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THE QUARTERLY REVIEW of BIOLOGY

INTEGRATIVE CARDIOVASCULAR PHYSIOLOGY: A MATHEMATICAL SYNTHESIS OF CARDIAC AND BLOOD VESSEL HEMODYNAMICS

BY FRED S. GRODINS

Northwestern University Medical School, Chicago

ABSTRACT

The cardiovascular system is analyzed as a feedback regulator. The controlling system is identified as being the medullary cardiovascular centers as well as those endocrine glands which operate upon the heart and blood vessels; the controlled system comprises the mechanical and gas exchanger elements of the cardiovascular system. The present analysis is restricted to the mechanical section of the controlled system. Equations are first formulated to define the steady-state operation of an isolated ventricle and of an isolated "circuit." Two ventricles are then combined with a single "open" circuit, the pulmonary, to obtain equations describing the operation of the Starling heart-lung preparation. Finally, the system is "closed" by introducing a second circuit, the systemic, and equations are obtained for the behavior of this complete mechanical system. These equations define steady-state values for each of the system's dependent variables (cardiac output; ventricular volumes and work; systemic arterial and venous pressures; pulmonary arterial and venous pressures; systemic and pulmonary blood volumes and their distribution between artery and vein) for any given set of values for the 14 independent variables (cardiac frequency; "strength," viscance, and compliance of each ventricle; systemic and pulmonary arteriolar resistances; systemic arterial and venous compliances; pulmonary arterial and venous compliances; and total blood volume). Comparison of predicted behavior with experimental data indicates that the mathematical model so obtained is a useful one.

INTRODUCTION

THE past ten years have witnessed an intensive reexamination of our ideas about cardiac output regulation (Stead and Warren, 1947; Hamilton, 1953, 1955; Katz, 1955; Sarnoff, 1955; Guyton, 1955; Gregg, Sabiston, and Theilin, 1955; Rushmer, 1955, 1956; Gauer, 1955; Richards, 1955). Controversies which have arisen, some real and some only apparent, have served to emphasize the need for a basic integration of cardiovascular dynamics. The present work attempts to provide its beginnings.

We have called this study a mathematical synthesis rather than a new theory because it is primarily the language which is new. For the most part, we shall simply translate into somewhat different form concepts and ideas which have been advanced and discussed by many workers over many years (Hamilton, 1953, 1955; Katz, 1955; Sarnoff, 1955; Guyton, 1955; Gregg, Sabiston, and Theilin, 1955; Rushmer, 1955, 1956; Gauer, 1955; Richards, 1955; Markwalder and Starling, 1914; Patterson and Starling, 1914; Patterson, Piper, and Starling, 1914, and Wiggers and Katz, 1922). In so doing, we shall construct a guide which will enable us to explore validly the implications of these concepts. Such a guide is indispensible in dealing with a complex multivariate system, and its absence has contributed in no small degree to some of the current controversies.

THE CARDIOVASCULAR SYSTEM AS A FEEDBACK REGULATOR

Let us begin by attempting to fit our system into the general pattern of a feedback regulator (Grodins, 1955, and Grodins, Gray, Schroeder, Norins, and Jones, 1954). We make a first major subdivision into a *controlling system* and a *controlled system*. The former consists of the medullary cardiac and vasomotor centers as well as those endocrine glands which operate upon the heart and blood vessels; the latter comprises the mechanical and gas exchanger elements of the cardiovascular system. In general, one or more outputs of the controlled system (the "controlled quantities") will feed back to provide input to the controlling system; and the output of the latter will influence one or more properties of the controlled system ("compensating" or "manipulated" quantities). The system may be "forced" (stimulated, driven, activated) either by "command" quantities entering the controlling system or by "load" quantities entering the controlled system. Without any more specific identification of these quantities, we summarize the general organization of the system in the block diagram of Fig. 1.

To understand such a system, we must first isolate its component parts, identify the inputs and outputs of each, and determine the laws defining the dependence of output on input. Having done this (but not before!) we can reassemble the parts into an operating regulator. Within this general framework, we can now define the limited scope of the present study. We shall deal only with the isolated mechanical section of the controlled system. We shall attempt to identify its inputs and outputs, formulate the laws which relate them, and examine the implication of these laws.

CONTROLLED SYSTEM—MECHANICAL SECTION

General survey

The mechanical elements of the cardiovascular regulator include the heart, and the arteries, arterioles, capillaries, and veins which comprise the "circuit." The heart consists of two pumps (left and right) and the "circuit" of two sections (systemic and pulmonary) arranged in series. Both systemic and pulmonary circuits consist of many distributed parallel elements. Let us first break down this complex system into manageable components for analysis and identify the inputs and outputs of each.

Looking first at the heart, we find the basic prototype in the "isolated ventricle" preparation. Here the physiological circuit is replaced by a controllable artificial system. The investigator can arbitrarily set the venous filling pressure, the mean arterial load pressure, and the cardiac frequency and thus can study the influence of each upon cardiac output and ventricular volumes. We thus identify the inputs (independent variables) as venous pressure, P_V , mean arterial pressure, P_A , and cardiac frequency, F. The outputs (dependent variables) are the ventricular volumes (diastolic, v_d ; residual, v_r ; stroke, v_s) and the cardiac output, Q. The unqualified terms "cardiac output," or "pump output" will refer to *a volume flow rate* whose general symbol will be Q. The appropriate block diagram is shown in Fig. 2.

Let us next examine the simplest sort of isolated circuit preparation. It would consist of a single circuit, either pulmonary or systemic, separated from all neurohumoral control and provided with a single mechanical pump to transfer blood at an arbitrary rate, Q, directly from central vein to central artery. We identify the system input as the pump output, Q, and the system outputs as the arterial and venous pressures, P_A and P_V , and blood volumes, V_A and V_V . The appropriate block diagram is shown in Fig. 3, and we note that the roles of Q, P_A , and P_V as input and output are the reverse of those in Fig. 2.

We next consider a variant of this single circuit. Instead of a single pump transferring blood directly from central vein to central artery, let us introduce two pumps, one of which transfers blood from an

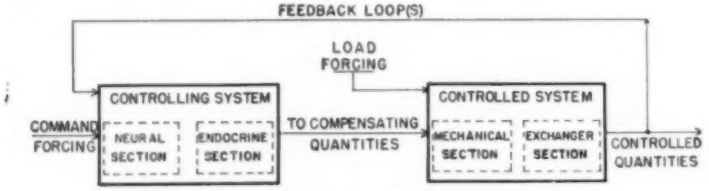

FIG. 1. THE CARDIOVASCULAR REGULATOR

external infinite source into the artery, while the other moves blood from the central vein to an external drain. If we require the outputs of the two pumps to be equal at every instant, then the new circuit behaves exactly as the old one did, and our modification is meaningless. If, however, we permit transient inequalities between the pump outputs, the total blood volume, B, in the circuit now becomes a dependent variable whereas it was previously independent. Accordingly, we shall call this variant an "open volume" circuit in contrast to the "closed volume" circuit previously described. The block diagram of the modified circuit appears in Fig. 4, where the outputs of the two pumps are Q_L and Q_R respectively.

Suppose we now use these heart and circuit building-blocks to construct the familiar Starling heart-lung preparation (Patterson and Starling, 1914). We start with two hearts, a left and a right. The three arbitrary inputs to this pair are now (1) the frequency, identical for both, (2) the venous filling pressure (systemic, P_{V_S}) for the right heart, and (3) the arterial load pressure (systemic, P_{A_S}) for the left heart. The outputs of these hearts, Q_L and Q_R, provide the input to the pulmonary circuit. The pressure outputs of this circuit feed back to provide the venous filling pressure (pulmonary, P_{V_P}) for the left heart and the arterial load pressure (pulmonary, P_{A_P}) for the right. Both these pressures are now dependent variables. The corresponding block diagram in Fig. 5 reveals that the Starling heart–lung preparation is already a fairly complex system.

One step remains to complete our initial picture of the mechanical section of the controlled system. We need only to close the system by introducing a second circuit, the systemic. The final block diagram is shown in Fig. 6. It reveals that the heart outputs, ventricular volumes, pulmonary pressures and volumes, and systemic pressures and volumes have all become dependent variables. Indeed, the only independent variable appearing in the diagram is the cardiac frequency, F. Actually, we have yet to identify an entire set of cardiac and circuit properties which will provide the remaining independent variables for this system. Some or all of these will play the role of "compensating quantities," "load quantities," or both in the intact regulator. To identify them we must now turn to a more detailed analysis of the mechanical system just surveyed. We begin with the isolated ventricle.

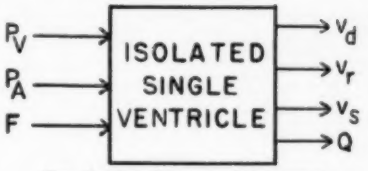

FIG. 2. THE ISOLATED VENTRICLE

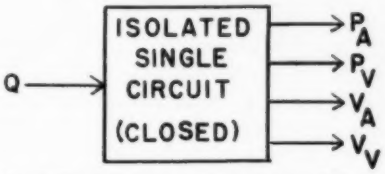

FIG. 3. THE ISOLATED "CLOSED-VOLUME" CIRCUIT

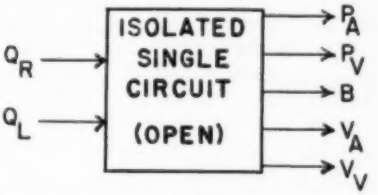

FIG. 4. THE ISOLATED "OPEN-VOLUME" CIRCUIT

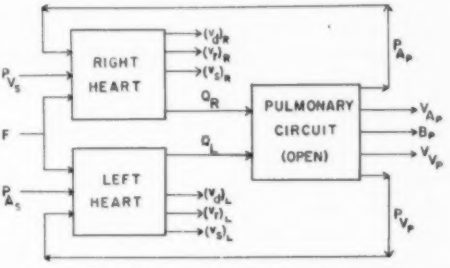

FIG. 5. THE STARLING HEART-LUNG PREPARATION

The isolated ventricle

We shall analyze the steady-state operation of the isolated ventricle in terms of an "emptying process" and a "filling process." Starting with the former, we suppose that we can isolate a single ventricular systole. At its beginning, the ventricle has a certain arbitrary diastolic volume, v_d. It then ejects a certain stroke volume, v_s, against an arbitrary mean arterial load pressure, P_A, thus leaving behind when systole is over a certain residual volume, v_r. We wish to define the dependence

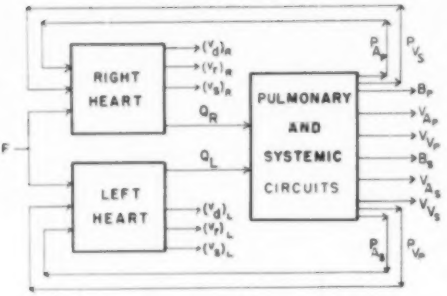

FIG. 6. THE COMPLETE MECHANICAL SYSTEM

of v_s and v_r upon the independent variables, v_d and P_A. To do so, we use Starling's "Law of the Heart" (Patterson, Piper, and Starling, 1914). We neglect any differences between "input loads" and "resistance loads" and restrict our operation to the region of "compensation." We assume that within this range, useful stroke work, w_s, is directly proportional to diastolic volume:

$$w_s = Sv_d \tag{1}$$

where the proportionality constant, S, will be called the "strength" of the ventricle. Equation (1) thus defines a one parameter family of "Starling curves" with parameter, S. Neglecting kinetic work as negligibly small, we equate w_s to the product of stroke volume and mean arterial pressure:

$$w_s = v_s P_A \tag{2}$$

Combining (1) and (2) to eliminate w_s gives

$$v_s P_A = Sv_d \tag{3}$$

and solving for v_s:

$$v_s = (S/P_A)v_d \tag{4}$$

and since

$$v_r = v_d - v_s \tag{5}$$

we have

$$v_r = [1 - (S/P_A)]v_d \tag{6}$$

Equations (4) and (6) define the emptying process. The ratio, (S/P_A), is the fraction of the diastolic volume discharged during systole, and since this cannot exceed unity, these equations are restricted to the range $(S/P_A) \leqq 1$. If $(S/P_A) > 1$, then we have simply $v_s = v_d$ and $v_r = 0$. Note that time does not appear in these equations: we are not concerned here with the kinematics of ejection, and Starling's law has nothing to say about this.

Turning to the filling process, we find our knowledge to be fragmentary, with more definitive studies only now beginning to reappear (Gauer, 1955; Buckley, Sidkey, and Ogden, 1956; Brecher, 1954, 1956; and Brecher and Kessen, 1957). To define the problem let us suppose that we can isolate a single ventricular diastole. At the start, the ventricle has a certain arbitrary residual volume, v_r. It then fills for an arbitrary length of time, t, at the end of which its volume will be the diastolic volume, v_d. We wish to define the dependence of v_d upon v_r, t, and the mechanical forces which drive and oppose filling. This is a formidable task, and no really satisfactory solution is presently attainable. Thus, the contribution of atrial systole may vary (Gauer, 1955; Wiggers and Katz, 1922). The mechanical properties of the ventricle during diastole are probably both non-linear and time-dependent (Buckley, Sidkey, and Ogden, 1956; and Brecher and Kessen, 1957). Recent evidence suggests that a ventricle operating at very small residual volumes exerts a "suction" action to aid filling (Brecher and Kessen, 1957). It seems unwise to attempt to include all of these complicating factors in the present analysis, particularly since many of their details remain to be worked out. Let us, therefore, work with a very simple filling law. We shall neglect any atrial contribution and assume (1) that ventricular relaxation occurs instantaneously at the end of systole and is thus complete before filling begins, (2) that filling of the relaxed ventricle is a first order linear process driven by a constant venous pressure and opposed by visco-elastic forces generated within the heart, and (3) that the unstressed volume of the relaxed ventricle is zero. These assumptions yield a filling law which turns out to be very useful in accounting for many observed features of overall system behavior, even though it neglects certain obvious details.

Filling laws incorporating time-dependent ventricular properties are described in Appendix 1.

The appropriate differential equation is:

$$RC\dot{v}_d + v_d = CP_V \tag{7}$$

where v_d is the diastolic volume at time, t, P_V is the venous filling pressure, C is the compliance of the relaxed ventricle, and R is the total viscous

resistance to filling including "bloodway" as well as "tissue" viscance. Both R and C are assumed to be linear and time-invariant. Since $v_d = v_r$ (the residual volume) at $t = 0$ (start of filling), we write the solution of (7) as follows:

$$v_d = CP_V + (v_r - CP_V)e^{-t/RC} \quad (8)$$

Equation (8) is our filling law defining the dependence of diastolic volume upon residual volume, venous filling pressure, filling time, and the compliance and viscance of the pump.

To define the steady-state operation of the isolated ventricle, we now combine filling and emptying processes. When we do this, t in equation (8) becomes a function of cardiac frequency, F. Let us assume that within our operating range, systole has a constant duration of 0.2 second so that

$$t = (60/F) - 0.2 \quad (9)$$

where F is expressed in cycles per minute and t in seconds. To simplify our notation, we define:

$$K \equiv e^{-[(60/F) - 0.2]/RC} \quad (10)$$

$$A \equiv 1 - K \quad (11)$$

Substituting (6) and (9) into (8), and incorporating definitions (10) and (11) yields the following equation for v_d:

$$v_d = CAP_V/1 + K[(S/P_A) - 1] \quad (12)$$

Note that equation (8) describes the filling transient, whereas, (12) defines the steady state value of v_d in the operating ventricle. From (4) and (12) it follows that

$$v_s = SCAP_V/AP_A + SK \quad (13)$$

and from (5), (12), and (13):

$$v_r = CAP_V(P_A - S)/AP_A + SK \quad (14)$$

The cardiac output, Q, is:

$$Q = Fv_s \quad (15)$$

so that finally:

$$Q = FSCAP_V/AP_A + SK \quad (16)$$

Let us briefly examine some implications of these equations. If P_V alone is increased, the equations say that v_d, v_s, v_r, and Q will all increase in direct proportion. If P_A is increased from S toward infinity, both v_s and Q will decrease hyperbolically to approach zero, while both v_d and v_r will increase hyperbolically to approach CP_V. A combination of these two forcings is commonly employed in heart-lung studies, i.e., as P_A is raised, P_V is also raised to keep v_s and Q constant. Under these conditions, the equations predict that P_V should be a positive linear function of P_A. The effect of frequency is particularly interesting. According to equation (16), Q will increase to a maximum, then fall again as F increases. By differentiating (16) with respect to F, we can show that this "optimum frequency," F_O, is independent of P_V but increases when the ratio, (S/P_A), or the "time constant," RC, decreases. Although F_O is independent of P_V, the actual value of Q at this frequency is not. In heart-lung studies, it is common, as F is increased, to manipulate P_V in order to keep Q constant. Under these conditions, our equations say that P_V must be decreased to a minimum, then increased again as F is raised. The minimum P_V occurs at F_O, i.e., at the (optimum) frequency for maximizing cardiac output with P_V constant. Having thus analyzed the operation of the isolated ventricle, let us turn now to our second basic building block, the isolated single circuit.

Isolated circuit

We begin by making a number of simplifying assumptions. We represent many parallel and distributed elements by a single equivalent circuit with lumped constants, assume that all components are linear, and neglect any kinetic energy of the blood as well as fluid exchange across the capillaries. If we deal in particular with the systemic circuit, we will then have two pure linear volume compliances (systemic "artery," C_{AS}, and systemic "vein," C_{VS}) connected peripherally by a pure linear (Poiseuille) resistance (systemic arterioles, R_S), and centrally by a mechanical pump which transfers blood at an arbitrary rate, Q, from "vein" to "artery." The volume flow rate, F_S, through R_S is then given by

$$F_S = (P_{AS} - P_{VS})/R_S. \quad (17)$$

The arterial and venous pressures are proportional to the volumes of blood contained within these vessels, and neglecting any blood in the pump, the sum of these volumes must equal the total systemic blood volume, B_S. Accordingly we write:

$$P_{AS} = (1/C_{AS})V_{AS} \quad (18),$$

(neglecting the fact that the unstressed arterial

volume is greater than zero), and

$$P_{V_S} = (1/C_{V_S})V_{V_S} \tag{19}$$

$$B_S = V_{A_S} + V_{V_S} \tag{20}$$

Finally we write the single steady-state restriction under which the system will operate:

$$Q = F_S \tag{21}$$

We now combine (17)-(21) to obtain equations defining the pressure outputs of the circuit as functions of Q and circuit properties (the "circuit properties" are B_S, R_S, C_{A_S}, and C_{V_S}):

$$P_{A_S} = (B_S/C_{A_S} + C_{V_S}) + (C_{V_S}R_SQ/C_{A_S} + C_{V_S}) \tag{22}$$

$$P_{V_S} = (B_S/C_{A_S} + C_{V_S}) - (C_{A_S}R_SQ/C_{A_S} + C_{V_S}) \tag{23}$$

Briefly examining some implications of these equations, we note that if $Q = O$,

$$P_{A_S} = P_{V_S} = (B_S/C_{A_S} + C_{V_S}) = P_s \tag{24}$$

where P_s is the "mean systemic pressure" of Weber (1850), or the "static blood pressure" of Starr and Rawson (1940), or the "mean circulatory filling pressure" of Guyton (1955). If we now increase Q with circuit properties constant, P_{A_S} increases and P_{V_S} decreases in linear fashion. The limit of this process is obviously reached when $P_{V_S} = O$. If we keep B_S, C_{A_S}, C_{V_S}, and Q constant, then P_{A_S} increases and P_{V_S} decreases as linear functions of R_S.

Let us now examine the single "open volume" circuit in which the central artery is supplied from an infinite external source by one pump (say the "left"), and the central vein is emptied into an external drain by a second pump (say the "right"). As mentioned previously, this modification is meaningful only if we permit transient inequalities between the outputs of the two pumps. Under these conditions, the blood volume in the circuit, B_S, at any time, t, becomes dependent upon the time integral of these inequalities:

$$B_S = B_{S_O} + \int_0^t (Q_L - Q_R)\, dt \tag{25}$$

When such a system is in a steady state (for which there are now *two* independent restrictions: $Q_L = Q_R$ and $Q_L = F_S$), the pressure drop, $P_{A_S} - P_{V_S}$, is still uniquely determined by this steady state; but the blood volume, and thus the absolute values of these pressures, depend upon the past history of the system. Thus if we increase Q_L and Q_R from one steady state to another, P_{A_S} and P_{V_S} may both rise, both fall, or move in opposite directions depending on the transient path chosen.

Finally, we close the system once more by introducing a second circuit, the pulmonary, whose vein is drained by the left pump which continues to feed the systemic artery, and whose artery is supplied by the right pump which continues to drain the systemic vein. If $Q_L = Q_R = 0$, the "static blood pressure" becomes

$$P_O = P_{A_S} = P_{V_S} = P_{A_P} = P_{V_P} = B/C_{A_S} + C_{V_S} + C_{A_P} + C_{V_P} \tag{26}$$

where B is the total blood volume. The pulmonary and systemic blood volumes under these static conditions, B_{P_O} and B_{S_O}, are

$$B_{P_O} = (C_{A_P} + C_{V_P}/C_{A_S} + C_{V_S} + C_{A_P} + C_{V_P})B \tag{27}$$

$$B_{S_O} = (C_{A_S} + C_{V_S}/C_{A_S} + C_{V_S} + C_{A_P} + C_{V_P})B \tag{28}$$

and

$$B = B_P + B_S \tag{29}$$

Now suppose we start the pumps with the restriction that $Q_L = Q_R$ at every instant. Obviously, there can be no redistribution of blood volume between the two circuits, and each would behave as a single "closed volume" circuit with static pressure defined by (26) and with arterial and venous pressures uniquely determined by circuit properties and pump output. (The *total* blood volume, B, not its parts, is now an independent circuit property.) But suppose we allow transient inequalities between Q_L and Q_R. Then:

$$B_S = B_{S_O} + \int_0^t (Q_L - Q_R)\, dt \tag{25}$$

$$B_P = B_{P_O} - \int_0^t (Q_L - Q_R)\, dt \tag{25a}$$

and each circuit behaves as a single "open volume" circuit with the restriction that $\Delta B_S = -\Delta B_P$. When such a system is in a steady state (for which there are now three independent restrictions: $Q_L = Q_R$; $Q_L = F_S$; $Q_R = F_P$), the pressure drops,

$P_{AS} - P_{VS}$ and $P_{AP} - P_{VP}$ are uniquely determined by this steady state; but the distribution of B between B_S and B_P, and thus the absolute values of all four pressures, depend upon the past history of the system. In the cardiovascular system, transient inequalities between left and right heart outputs do occur, and in so doing introduce a dissociation between static and dynamic intercircuit blood distributions, but because ventricular outputs are in part dependent upon circuit pressures, we can still specify unique steady states without knowledge of the preceding transients.

Having now analyzed our basic mechanical components, we are ready to synthesize them into more complex systems. We begin with the Starling heart-lung preparation (Patterson and Starling, 1914).

The Starling heart-lung preparation

This preparation combines a conventional single "open volume" circuit with two special pumps whose outputs are in part dependent upon the circuit pressures. Because of this dependence, the system manifests what we shall call "mechanical self-regulation," and the steady-state cardiac output, circuit blood volume, and circuit pressures are all uniquely determined for any given set of inputs (P_{VS}, P_{AS}, F), cardiac properties (S_L, S_R, C_L, C_R, R_L, R_R), and circuit properties (R_P, C_{AP}, C_{VP}). The necessity for knowledge of the pump output transients in order to specify the steady-state circuit pressures is thereby removed. Let us see how this works out.

First we specialize equations (1)–(8) and (10)–(16) to apply to the left ventricle, then write an identical set for the right ventricle and indicate by subscript which one we are dealing with. Equation (9) is common to both. The appropriate symbols for the left side then become: $(w_s)_L$, $(v_d)_L$, $(v_s)_L$, $(v_r)_L$, Q_L, S_L, C_L R_L, K_L, A_L, P_{VP}, and P_{AS}, and for the right: $(w_s)_R$, $(v_d)_R$, $(v_s)_R$, $(v_r)_R$, Q_R, S_R, C_R, R_R, K_R, A_R, P_{VS}, and P_{AP}. We will not need to rewrite these equations but will simple indicate their corresponding numbers:

Left Ventricle	*Right Ventricle*
(1)–(8)	(30)–(37)
(9)	(9)
(10)–(16)	(38)–(44)

Next, we change the symbols of circuit equations (17)–(20) to apply to the pulmonary circuit:

$$F_P = (P_{AP} - P_{VP})/R_P \tag{45}$$

$$P_{AP} = (1/C_{AP})V_{AP} \tag{46}$$

$$P_{VP} = (1/C_{VP})V_{VP} \tag{47}$$

$$B_P = V_{AP} + V_{VP} \tag{48}$$

and finally write the two steady-state restrictions under which this system will operate:

$$Q_L = Q_R = Q \tag{49}$$

$$Q_R = F_P \tag{50}$$

Now if we consider equations (1), (2), (5), (8), (9), and (15) for the left ventricle, their counterparts for the right ventricle, (30), (31), (34), (37), (9), and (43), and circuit equations (45)–(50), we discover that we have seventeen independent simultaneous equations (Equation 9, being identical for both ventricles, is counted only once) in seventeen unknowns ($(w_s)_L$, $(w_s)_R$, $(v_d)_L$, $(v_d)_R$, $(v_r)_L$, $(v_r)_R$, $(v_s)_L$, $(v_s)_R$, t, Q_L, Q_R, F_P, P_{AP}, P_{VP}, V_{AP}, V_{VP}, B_P). This set is thus necessary and sufficient to define a unique steady state for any given set of values for the three inputs (P_{VS}, P_{AS}, F) and nine system properties (S_L, S_R, C_L, C_R, R_L, R_R, R_P, C_{AP}, C_{VP}). We can combine these equations in various ways; but the form in which we put the solutions will be dictated by the types of experimental observations which have been made in the heart-lung preparation, for it is at this point that we wish to make a major comparison between theory and experiment to see if our model is in any way a faithful one. Three experimental procedures are commonly used, each of which yields a relationship between two variables under specified conditions:

(1) Cardiac output and cardiac frequency are kept constant while systemic arterial pressure is varied. To keep Q constant, the systemic venous pressure must be manipulated. Hence, one can obtain a relationship between P_{VS} and P_{AS} with Q and F constant.

(2) Cardiac frequency and systemic arterial pressure are kept constant while systemic venous pressure is varied. This produces changes in cardiac output so that one can obtain a relationship between Q and P_{VS} with F and P_{AS} constant.

(3) Cardiac output and systemic arterial pressure are kept constant while cardiac frequency is varied. To keep Q constant, systemic venous pres-

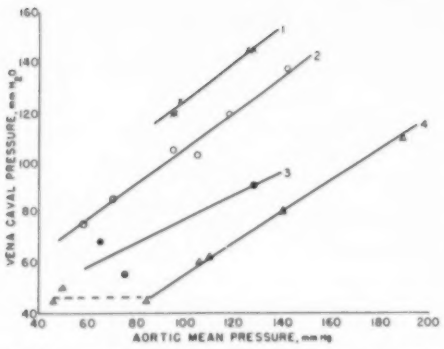

FIG. 7. RELATIONSHIP BETWEEN P_{V_S}, AND P_{A_S} WITH Q AND F CONSTANT IN HEART-LUNG PREPARATION

sure must be manipulated. Hence, one can obtain a relationship between P_{V_S} and F with Q and P_{A_S} constant.

Let us therefore put our equations into forms which correspond to each of these experimental procedures:

$$P_{V_S} = [Q^2/F^2S_LS_RC_LC_R]P_{A_S} + [(R_PQ^2/FS_RC_R) + (K_LQ^2/F^2S_RC_LC_RA_L) + (K_RQ/FC_RA_R)] \quad (51)$$

$$P_{V_S} = [K_R/FC_RA_R]Q + [(P_{A_S}/F^2S_LS_RC_LC_R) + (R_P/FS_RC_R) + (K_L/F^2S_RC_LC_RA_L)]Q^2 \quad (52)$$

$$P_{V_S} = [(R_PQ^2/S_RC_R) + (K_RQ/C_RA_R)][1/F] + [(Q^2P_{A_S}/S_LS_RC_RC_L) + (Q^2K_L/S_RC_LC_RA_L)][1/F^2] \quad (53)$$

Equation (51) says that P_{V_S} is a linear function of P_{A_S} when Q and F are constant. Equation (52) (in which independent and dependent variables have been reversed for convenience) says that P_{V_S} is a parabolic function of Q when P_{A_S} and F are constant. Equation (53) is not a simple function since the independent variable, F, appears both algebraically and transcendentally (hidden in K_L, A_L, K_R, A_R). The complexity of this relationship is not surprising. Thus we have shown that in the single ventricle preparation, P_V passes through a minimum at a certain frequency, F_O. In general, this frequency will not be identical for the two ventricles operating together in the Starling preparation. However, we can show that (53) also defines a curve which passes through a minimum at a frequency which depends upon certain system properties. With this background, let us now compare theory with experiment. We begin with equation (51).

The relationship between systemic venous and arterial pressures with Q and F constant obtained in four heart–lung experiments by Patterson, Piper, and Starling, (1914) is shown in Fig. 7. The predicted positive linear relationship is reasonably well confirmed. The lowest curve demonstrates the discontinuity predicted by the theory at the point $S/P_A = 1$. Let us attempt to use these curves, together with some independent information and a few reasonable assumptions, to evaluate some of our system properties. From equation (51), the slope of the curve, dP_{V_S}/dP_{A_S}, is:

$$dP_{V_S}/dP_{A_S} = v_s^2/S_LS_RC_LC_R \quad (54)$$

Now dP_{V_S}/dP_{A_S} and v_s are known. We evaluate C_L and C_R from the linear portion of the static volume-pressure curves reported by Brecher and Kessen (1957), as 2.45 and 4.75 cc/mm Hg respectively. We next assume that the ratio S_L/S_R is equal to the normal ratio of the respective arterial load pressures, and we take the latter as approximately 5/1. Then using curve 2, whose slope is 0.053 mm Hg P_{V_S}/mm Hg P_{A_S}, we obtain 18.5 mm Hg for S_L and 3.7 mm Hg for S_R. Consider now the intercept constant of (51). The quantities still unknown are R_P, K_L, A_L, and A_R. Let us assign 0.002 mm Hg/cc/min as a reasonable value for R_P, and assume that $R_LC_L = R_RC_R$ so that $K_L = K_R$ and $A_L = A_R$. Then using the measured (extrapolated) intercept of curve 2, we obtain $K_L = K_R = 0.45$ and $A_L = A_R = 0.55$. At $F =$ 138 cpm, these correspond to a "time constant" of 0.29 second, a reasonable value. Suppose we now use these values to determine how successfully our theory predicts the behavior of the ventricular volumes which were also recorded in this particular experiment.

Since the reported cardiometer tracings represent the sum of left and right ventricular volumes, we need an equation in this form. It is not difficult to show that:

$$(v_d)_{L+R} = [(v_s/S_L) + (v_s^2/S_LS_RC_L)]P_{A_S} + [(v_sQR_P/S_R) + (v_s^2K_L/S_RC_LA_L)] \quad (55)$$

Substituting appropriate numerical values, this becomes:

$$(v_d)_{L+R} = 0.25P_{A_S} + 7 \quad (56)$$

It is then obvious that:

$$(v_r)_{L+R} = (v_d)_{L+R} - 2v_s = 0.25P_{AS} - 6 \quad (57)$$

In Fig. 8 we have plotted equations (56) and (57) together with the experimentally determined cardiometer values. Unfortunately, the zero point of the cardiometer record is unknown, so we force theory and experiment to coincide at one point ($P_{AS} = 118$) and use the other three as a test for the adequacy of the theory. Agreement is good except at the highest pressure value, which may be getting beyond our restricted operating range. The absolute values of the ventricular volumes appear to be of the correct order of magnitude. We conclude that the mathematical model is faithful in predicting the response of the Starling preparation to this particular forcing. Let us turn now to the second type of experiment.

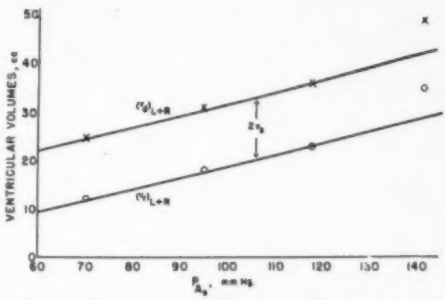

FIG. 8. DIASTOLIC AND RESIDUAL VOLUMES AS FUNCTIONS OF P_{AS} IN THE HEART-LUNG PREPARATION WITH Q AND F CONSTANT

In Fig. 9 is plotted the relationship between systemic venous pressure and cardiac output obtained in five experiments on four heart-lung preparations by Patterson and Starling (1914). Although P_{AS} and F were constant within 20 per cent for each experiment, variation in F between experiments was somewhat wider. Individual experiments, as well as the group as a whole, show a curvilinear relationship similar to that demanded by theory. Averaging the indicated groups of points and plotting (P_{VS}/Q) against Q for these means yields, with only one aberrant point, the excellent linear relationship shown in Fig. 10. This successful rectification indicates the parabolic nature of the original data. The following parabola was, therefore, fitted to the mean points (the circled point not included), and is plotted in Fig. 11:

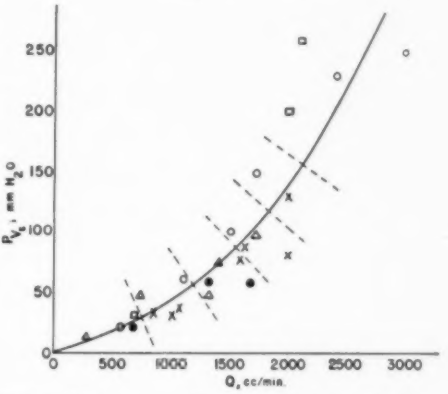

FIG. 9. RELATIONSHIP BETWEEN P_{VS} AND Q WITH P_{AS} AND F CONSTANT IN THE HEART-LUNG PREPARATION

$$P_{VS}(\text{mm } H_2O) = 0.006Q + (3.8 \times 10^{-5})Q^2 \quad (58)$$

From equations (52) and (58), after changing the P_{AS} units in the latter to mm Hg, we have

$$K_R/FC_RA_R = 4.41 \times 10^{-4} \quad (59)$$

The mean F for the present experiments was 144 cpm, and assuming again that $C_R = 4.75$ cc/mm Hg, we evaluate K_R as 0.232, A_R as 0.768, R_RC_R as 0.15 second, and R_R as 3.16×10^{-2} mm Hg/cc/sec (5.3×10^{-4} mm Hg/cc/min). Again from (53) and (58) we have

$$(P_{AS}/F^2S_LS_RC_LC_R) + (R_P/FS_RC_R) + (K_L/F^2S_RC_LC_RA_L) = 2.95 \times 10^{-6} \quad (60)$$

The mean P_{AS} for the present experiments was 90 mm Hg. Again taking C_L as 2.45 cc/mm Hg, R_P as 0.002 mm Hg/cc/min, and assuming $K_L = K_R$ and $S_L = 5S_R$, we evaluate the remaining properties as: $R_L = 1.02 \times 10^{-3}$ mm Hg/cc/min, $S_L = 30$ mm Hg, and $S_R = 6$ mm Hg.

It thus appears that the model can successfully account for the observed curvilinear relationship between P_{VS} and Q using constants of a reasonable order of magnitude. The curvilinearity predicted by theory depends upon the fact that an arbitrary increase in the independent variables, P_{VS}, produces an increase in the dependent variable, P_{AP}, thus imposing a double load upon the right ventricle. It is this double load which dictates the curvilinear relation between P_{VS} and Q even in the restricted region where stroke work is linearly dependent upon diastolic volume. That P_{AP} does

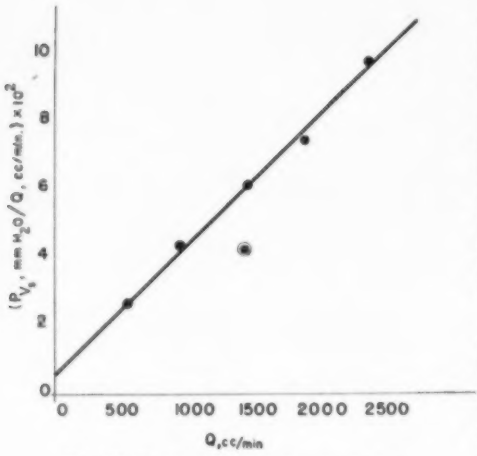

FIG. 10. DATA OF FIG. 9 AVERAGED AND RECTIFIED BY A RECIPROCAL PLOT

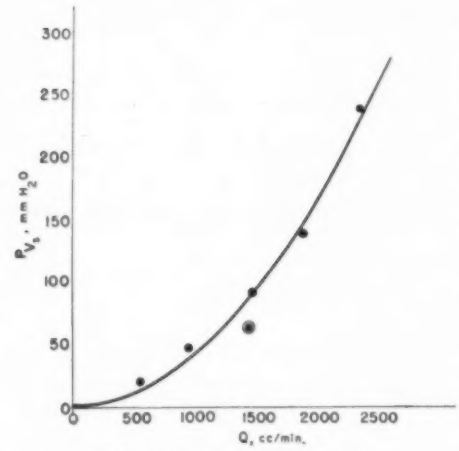

FIG. 11. PARABOLA FITTED TO AVERAGED DATA OF FIG. 9

in fact rise in this type of heart-lung experiment appears reasonably well established (Führer and Starling, 1913; Kuno, 1915). But we must briefly examine at least two obvious alternative explanations for this curvature. Although our assumption that $w_s = Sv_d$ is a reasonable approximation at small and moderate work loads, we know that eventually dw_s/dv_d must begin to decrease. If this happened, then the P_{V_S} versus Q relation would begin to curve even if P_{A_P} did not rise; and if P_{A_P} did rise, the curvature would simply be exaggerated. That this explanation is unlikely in the present experiments (except perhaps when $P_{V_S} >$ 150 mm H_2O) is indicated by the facts (1) that the curvature is already apparent in the lowest work ranges, and (2) that it occurs in the same work range in which the P_{V_S} vs. P_{A_S} relation previously discussed is linear. If a non-linear emptying law were operating, both, not just one of these relationships, should be curvilinear. The same considerations also serve to minimize the importance of a non-linear filling impedance.

This leads us directly to a second controversial point. In our model, an arbitrary increase in the independent variable, P_{A_S}, requires that we increase P_{V_S} to keep Q constant only because the dependent variable, P_{A_P}, also rises, thus imposing an "emptying load" on the right as well as on the left ventricle. The rise in P_{A_P} is associated with an equal rise in P_{V_P}. In short, our model under these conditions manifests what has been called "back pressure" (Wiggers, 1921). If it did not, there would be no reason to require an increase in P_{V_S}. Does "back pressure" occur in the heart-lung preparation? Opinions vary, and if we examine some of them carefully, it appears that we are asked to accept certain incompatible ideas as simultaneously true (Anrep and Bulatao, 1925). First, there is general agreement that if we increase P_{V_S} with P_{A_S} and F constant ("increased venous inflow"), P_{A_P}, P_{V_P}, and of course Q all rise (Patterson and Starling, 1914; Führer and Starling, 1913; Kuno, 1915). Apparently "forward pressure" effects do occur. But now if we raise P_{A_S} while keeping either "venous inflow from the reservoir" or "systemic output" (Q minus coronary flow) constant, it is said that P_{A_P} rises but that P_{V_P} does not (Anrep and Bulatao, 1925). The rise in P_{A_P} is attributed to an increase in coronary flow and thus in Q, and "back pressure" is said not to occur (Anrep and Bulatao, 1925). But if this really eliminates the existence of "back pressure," it does so only by simultaneously eliminating "forward pressure," which everyone seems to agree does exist. We can hardly accept such evidence as conclusive, and pending further proof to the contrary, we shall still regard our model as a faithful one even though it permits back pressure. Moreover, there appears to be considerable evidence that back pressure does in fact occur in closed-circuit heart-lung preparations (Katz, Wise, and Jochim, 1945a, b, c).

Theory also predicts the behavior of the ven-

tricular volumes when P_{VS} is varied. It is easily shown that

$$(v_d)_{L+R} = (P_{AS}/FS_L)Q + [(R_P/FS_R) + (P_{AS}/F^2S_LS_RC_L) + (K_L/F^2S_RA_L)]Q^2 \quad (61)$$

The linear term represents $(v_d)_L$ and the square term $(v_d)_R$. Unfortunately, cardiometer records were not taken in the group of experiments plotted in Fig. 9. However, such a record is available from the heart which yielded the data for curve 1 in Fig. 7. Using the latter data and equation (51), we evaluate the constants for this heart as previously described: $S_L = 27.5$; $S_R = 5.7$; $K_L = 0.25$; $A_L = 0.75$. Using these values in equation (61), we obtain the theoretical volume curves of Fig. 12. The points are taken from the reported cardiometer records, theory and experiment being forced into agreement at $Q = 750$ cc/min. We would like to see more such data and somewhat better agreement, but tentatively conclude that our model is reasonably faithful in describing the responses of the heart-lung preparation to changes in P_{VS}.

Let us finally examine the third type of experiment. In Fig. 13 is plotted the relationship between systemic venous pressure and cardiac frequency obtained in two experiments by Markwalder and Starling (1914). Cardiac output and mean systemic arterial pressure were kept constant in each experiment. The data are obviously curvilinear, and the curvature is in the direction demanded by theory. To test the latter, the smooth curves in Fig. 13 were calculated from equation (53) by first assigning arbitrary values to $R_P(0.002)$, $C_L(2.45)$, $C_R(4.75)$, $R_LC_L = R_RC_R(0.3)$, assuming that $S_L = 5S_R$, and then solving equation (53) at one observed point to obtain the values for S_R and S_L. The entire curve could then be constructed. Thus theory and experiment were forced to coincide at a single point on each curve, and the extent of agreement over the rest of the range can be taken as a measure of the faithfulness of the theory. Agreement appears to be reasonably good for both experiments. However, there are some difficulties. Both experiments were done on the same heart-lung preparation within approximately an hour's time. It might be reasonable to expect that the ventricular strengths would remain fairly constant over this interval. To make our equations fit, however, we had to use strength values approximately 1.8 times as large for experiment *b* than for experiment *a*. Is there any plausible reason why such a

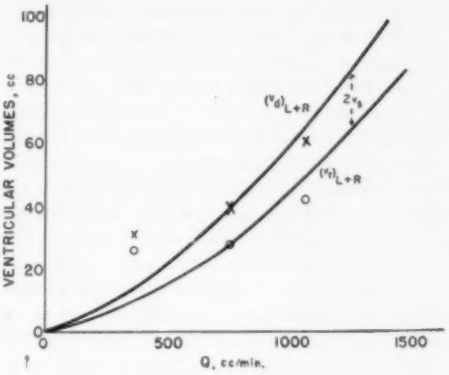

FIG. 12. DIASTOLIC AND RESIDUAL VOLUMES AS FUNCTION OF Q IN THE HEART-LUNG PREPARATION WITH P_{AS} AND F CONSTANT

difference should actually exist? If we look at the coronary sinus flows which were also measured in these experiments, we see that they are nearly twice as large in experiment *b* as in experiment *a*. If we said that this increased coronary flow was reason enough to account for the strength change, we would be in agreement with Starling's own ideas (Patterson, Piper, and Starling, 1914). It is not immediately obvious, however, why a proportionate increase in coronary flow *and* work output should increase myocardial strength. But even accepting this, we find other difficulties. If every increase in coronary flow, even though accompanied by an increase in work output, increases ventricu-

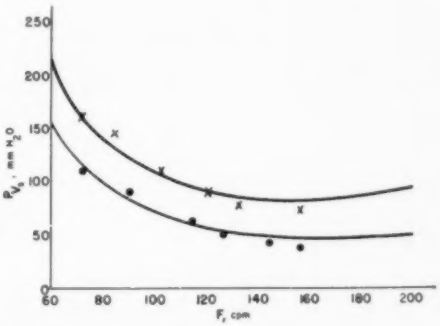

FIG. 13. SYSTEMIC VENOUS PRESSURE AS A FUNCTION OF F WITH Q AND P_{AS} CONSTANT IN THE HEART-LUNG PREPARATION. Circles, Experiment *a*; Crosses, Experiment *b*.

lar strength, then the latter could not have remained constant in either of the first two types of experiments considered. Yet the theory which assumed a constant strength was able to account for the observations. Perhaps we can safely assume that this particular heart is behaving in an unusual fashion. If we can judge from the two points available at relatively constant frequency, it does not appear to show the parabolic type of relationship between P_{V_S} and Q demonstrated by the four preparations in Fig. 9. The curvature should be even greater in the present case because both P_{A_S} and Q were higher in experiment b than in experiment a. Finally, we cannot ignore the fact that the frequency changes in these experiments were produced by altering the blood temperature over a range of eleven degrees centigrade (28–39°C). We have no independent evidence to insure that any or all of the cardiac properties (S, C, R) are independent of temperature. Thus, even though theory and observation agree reasonably well within a single experiment, there are many complicating factors emphasizing the need for additional experimental study. These same considerations also emphasize the difficulty of maintaining really effective control over cardiac properties even in a heart removed from neural and endocrine influences (Wiggers, 1921). Recognizing that more extensive studies are needed to provide a really adequate test for our mathematical model of the Starling preparation, we will assume that it is probably faithful enough to warrant exploring its extension to the complete mechanical system of Fig. 6.

The complete mechanical system

We now introduce into the Starling preparation a second circuit, the systemic, whose vein is drained by the right heart and whose artery is supplied by the left. We thus have two conventional "open volume" circuits, but they are connected in series through the same pair of special, pressure-dependent pumps. Because of this, the system manifests "mechanical self-regulation"; and its steady-state operation becomes definable without knowledge of previous pump transients. Although each component circuit is "open," the system as a whole is "closed," thus imposing the restriction, $\Delta B_S = -\Delta B_P$. To define the operation of this system, we must add six new equations to our previous set of seventeen. They are equations (17)–(20), already written for the isolated systemic circuit, (29), previously written for the isolated double circuit, and a third steady-state restriction:

$$Q_L = F_S \tag{62}$$

We also add six new unknowns (P_{A_S}, P_{V_S}, V_{A_S}, V_{V_S}, B_S, and F_S), thus obtaining a group of twenty-three independent simultaneous equations in twenty-three unknowns. This set is necessary and sufficient to define a unique steady state for any given set of values for the fourteen independent variables (F, S_L, S_R, C_L, C_R, R_L, R_R, R_P, C_{A_P}, C_{V_P}, R_S, C_{A_S}, C_{V_S}, and B).

Although we could solve for any one of the dependent variables, it is perhaps most convenient to obtain an equation in P_{A_S} only. This turns out to be an algebraic equation of sixth degree:

$$\theta P_{A_S}^6 + \lambda P_{A_S}^5 + \mu P_{A_S}^4 + \pi P_{A_S}^3 + \rho P_{A_S}^2 + \sigma P_{A_S} - \phi = 0 \tag{63}$$

[Details of derivation available upon request].

where the constants are rather complex functions of the system properties as defined below:

$$\theta \equiv -Ek^2 + an^2$$

$$\lambda \equiv -fk^2 + bn^2 + hkn - 2Ekl + 2anp$$

$$\mu \equiv -gk^2 + cn^2 + hkp + 2fkl + 2bnp + n(ik - hl) - E(l^2 - 2km) + ap^2$$

$$\pi \equiv + dn^2 + 2gkl + 2cnp + p(ik - hl) - f(l^2 - 2km) + bp^2 + n(jk - il - hm) - 2Elm$$

$$\rho \equiv + 2dnp - g(l^2 - 2km) + cp^2 + p(jk - il - hm) - 2flm - n(jl + im) - Em^2$$

$$\sigma \equiv + dp^2 - 2glm - p(jl + im) - fm^2 - jmn$$

$$\phi \equiv gm^2 + jmp$$

where:

$$a \equiv S_R C_R A_L^3 A_R$$

$$b \equiv 3S_L S_R C_R K_L A_L^2 A_R$$

$$c \equiv 3S_L^2 S_R C_R K_L^2 A_L A_R$$

$$d \equiv S_L^3 S_R C_R K_L^3 A_R$$

$$E \equiv S_L C_L A_L^3 A_R$$

$$f \equiv S_L^2 C_L A_L^2 A_R (2K_L + FC_L A_L R_P)$$

$$g \equiv S_L^3 C_L K_L A_L A_R (K_L + FC_L A_L R_P)$$

$$h \equiv S_L S_R C_L A_L^3 (K_R + FC_R A_R R_S)$$

$$i \equiv 2S_L^2 S_R C_L K_L A_L^2 (K_R + FC_R A_R R_S)$$

$$j \equiv S_L^3 S_R C_L K_L^2 A_L (K_R + FC_R A_R R_S)$$

$$k \equiv A_L (C_{V_S} + C_{A_S})$$

$$l \equiv [A_L B - S_L K_L (C_{V_S} + C_{A_S})]$$

$$m \equiv S_L K_L B$$

$$n \equiv A_L (C_{V_P} + C_{A_P})$$

$$p \equiv S_L K_L (C_{V_P} + C_{A_P}) + FS_L C_L A_L (C_{A_P} R_P - C_{V_S} R_S)$$

Solution of equation (63) by graphic or numerical methods is not difficult. It is somewhat laborious to calculate the constants for this equation, but with the groupings shown above, even this becomes a reasonable task. Once P_{A_S} has been obtained in this way, we can get P_{V_P} from the following expression:

$$P_{V_P} = (-kP_{A_S} + lP_{A_S} + m)/(nP_{A_S} + p) \quad (64)$$

then the cardiac output Q, from:

$$Q = Q_L = (FS_L C_L A_L P_{V_P})/(A_L P_{A_S} + S_L K_L) \quad (16)$$

and all other dependent variables follow rather obviously from the various basic equations of the system. It would be perfectly feasible to program this entire operation for a high speed digital computer.

It remains to examine the steady-state behavior of the system as predicted by our equations and to compare theory with experiment in so far as possible. In calculating the theoretical behavior, we have chosen to use parameter values "guessed" to be appropriate for an adult human cardiovascular system. This will not invalidate the qualitative comparisons which we shall make with experiment, even though the latter may have been carried out upon a "closed-circuit" dog heart-lung preparation (Katz, Wise, and Jochim, 1945a, b, c; Daly, 1925a, b); or an intact dog (Sarnoff and Berglund, 1954; Berglund, 1954). It is obvious that our present exploration cannot be exhaustive, for the number of possible qualitatively different forcings with fourteen independent variables which may be varied alone or in any combination is tremendous (4,782,954). Accordingly, we shall consider only a few examples of major interest.

1. *Normal Operating Point.* The set of parameter values arbitrarily chosen for a normal human adult at rest were: F = 75 cpm; S_L = 50 mm Hg; S_R = 7 mm Hg; C_L = 20 cc/mm Hg; C_R = 50 cc/mm Hg; R_L = 0.018 mm Hg/cc/sec; R_R = 0.007 mm Hg/cc/sec; C_{A_S} = 1 cc/mm Hg; C_{V_S} = 500 cc/mm Hg; C_{A_P} = 3 cc/mm Hg; C_{V_P} = 100 cc/mm Hg; R_S = 0.0167 mm Hg/cc/min; R_P = 0.001 mm Hg/cc/min; B = 5000 cc. This set of parameters yielded the following "normal" values for the dependent variables: Q = 6.5 L min; v_v = 86.6 cc; $(v_d)_L$ = 201 cc; $(v_r)_L$ = 114 cc; $(v_d)_R$ = 216 cc; $(v_r)_R$ = 129 cc; P_{A_S} = 116 mm Hg; P_{A_P} = 17.5 mm Hg; P_{V_S} = 7.5 mm Hg; P_{V_P} = 11.0 mm Hg; V_{A_S} = 116 cc [too low because positive unstressed volume is neglected]; V_{V_S} = 3750 cc; B_S = 3866; V_{A_P} = 52 cc; V_{V_P} = 1100 cc; B_P = 1152 cc. The pulmonary circuit thus contains approximately 23 per cent of the total blood volume. Due to minor inaccuracies in the graphic solution of equation (63) and to rounding errors, the above volumes sum to 5018 cc, an error of less than 0.4 per cent.

2. *Blood Volume Changes.* Fig. 14 shows the behavior of cardiac output, arterial and venous pressures, and the percentage of the total blood volume in the pulmonary circuit as the total blood volume is varied from 2000 to 8000 cc. The corresponding

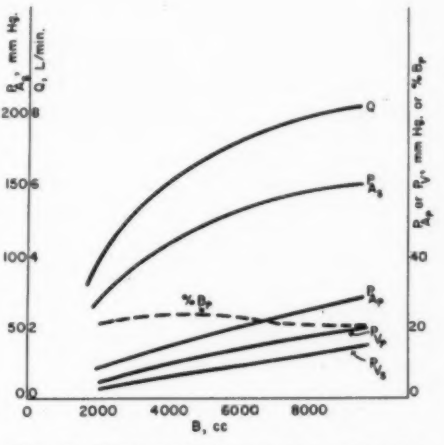

FIG. 14. THEORETICAL RESPONSES TO CHANGES IN BLOOD VOLUME

ventricular volumes are given in Fig. 15. This is perhaps the simplest forcing; and the theoretical predictions are in excellent qualitative agreement with experimental data obtained on the "closed circuit" heart-lung preparation by Daly (1925a) and by Katz, Wise, and Jochim (1945a,b), as well as in the intact dog by Sarnoff and Berglund (1954). The former preparation is the better one for our purposes, for it is probably unrealistic to assume that all of the system parameters except the blood volume remain constant in Sarnoff's studies.

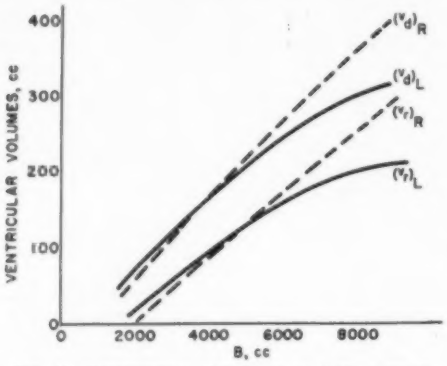

FIG. 15. THEORETICAL RESPONSE OF VENTRICULAR VOLUMES TO CHANGES IN BLOOD VOLUME

3. Peripheral Resistance Changes. Fig. 16 shows the behavior of cardiac output, arterial and venous pressures, and blood volume distribution when pulmonary (Fig. 16, left) or systemic (Fig. 16, right) resistance is varied from half "normal" to twice normal. The corresponding ventricular volumes are shown in Fig. 17. The two forcings have quite different effects. Cardiac output decreases with both, but much more rapidly with rising systemic resistance. When the latter rises both arterial pressures increase; but when pulmonary resistance is raised, systemic arterial pressure falls. Behavior such as this is impossible to predict without a mathematical guide, and is critically dependent upon system parameter values in ways which our equations precisely define. We can illustrate this

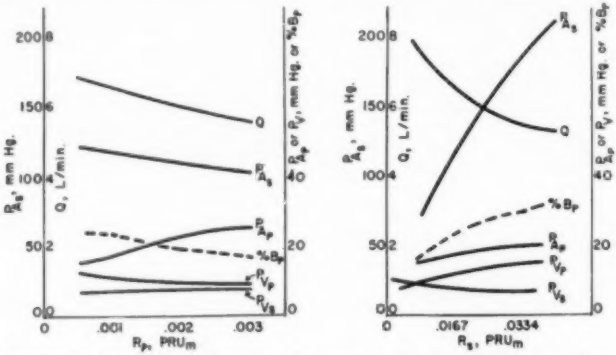

FIG. 16. THEORETICAL RESPONSES, LEFT, TO CHANGES IN R_P, AND RIGHT, TO CHANGES IN R_S

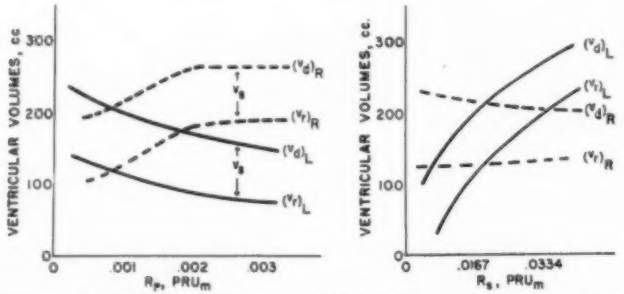

FIG. 17. THEORETICAL RESPONSE OF VENTRICULAR VOLUMES, LEFT, TO CHANGES IN R_P, AND RIGHT, TO CHANGES IN R_S

TABLE 1

The Effect of Doubling R_S at Four Different Values of C_{AS}

DEPENDENT VARIABLES	C_{AS} = 30 cc/mm Hg		C_{AS} = 20 cc/mm Hg		C_{AS} = 10 cc/mm Hg		C_{AS} = 1 cc/mm Hg	
	R_{SN}*	2 R_{SN}	R_{SN}	2 R_{SN}	R_{SN}	2 R_{SN}	R_{SN}	2 R_{SN}
Q, cc/min	4551	3158	5156	3793	5864	4589	6497	5428
P_{AS}, mm Hg	80	108	91	130	104	158	116	188
P_{VS}, mm Hg	4.0	2.5	4.9	3.3	6.1	4.7	7.5	6.7
P_{AP}, mm Hg	10.1	8.2	12.2	10.9	14.9	14.9	17.5	19.8
P_{VP}, mm Hg	5.5	5.0	7.0	7.1	9.0	10.3	11.0	14.4
v_s, cc	60.5	42	68.5	50.5	78	61	86.5	72.5
$(v_d)_L$, cc	97	91	125	131	160	193	201	272
$(v_d)_R$, cc	87	49	119	79	166	130	216	205
$(v_d)_{L+R}$, cc	184	110	244	210	326	323	417	477

* "Normal" R_S

nicely by making some comparisons with experimental data.

Daly (1925b) studied the effects of systemic peripheral resistance changes in a closed circuit heart-lung preparation for each of three different values of systemic arterial compliance. A rise in R_S always caused a rise in P_{AS} and a fall in Q. When C_{AS} was large, P_{VP}, P_{AP} and P_{VS} all fell, as did the ventricular volumes (cardiometer). As C_{AS} was given smaller values, the percentage fall in Q became less, the decrease in ventricular volumes was diminished or abolished, and P_{VP} began to rise. Let us see what our theory predicts in this situation. In Table 1 we give the theoretical effects of doubling R_S at each of four values for C_{AS}. The largest value, C_{AS} = 30, corresponds to Daly's "large potential capacity increment" of the systemic arterial system. Under these conditions, doubling R_S causes a large drop in Q (−30%) and in ventricular volumes (−40%), and a fall in all circuit pressures except P_{AS}. This agrees with observation. When C_{AS} = 20 ("moderate potential capacity increment") the percentage fall in both Q and ventricular volumes is less (−26% and −14% respectively); P_{VS} and P_{AP} still fall but to a lesser extent; and P_{VP} now begins to rise slightly, again in agreement with observation. Finally at C_{AS} = 10 ("small potential capacity increment"), the fall in Q is still less (−19%); the ventricular volumes remain nearly constant; the rise in P_{VP} becomes more pronounced; and P_{AP} now remains constant while P_{VS} continues to fall. Once more, theory and observation are in agreement. It therefore seems safe to extrapolate to C_{AS} = 1 (the particular value chosen for our "normal") and to assume that if Daly had used a still smaller "potential capacity increment," he would have found, as theory predicts, that ventricular volumes as well as P_{AP} were increased. Our predictions of the system responses to changes in R_S and R_P also appear to be in good agreement with the observations of Katz, Wise, and Jochim (1945a,b) in their closed circuit heart-lung preparation and to be capable of accounting satisfactorily for variations which they observed in the behavior of the various circuit pressures.

Although the intact animal is hardly an ideal subject for comparison, we may perhaps safely assume that the experimental forcings employed by Berglund, (1954) overwhelmed any controlling operations which the cardiovascular regulator may have initiated and so produced behavior resembling that of an isolated mechanical system. He examined the relationship between left and right atrial pressures as blood volume was increased under "normal" conditions, with the pulmonary artery constricted, or with the ascending aorta constricted. We can regard the latter two procedures as representing an increase in R_P and R_S respectively, although they are really more complex than this because the resistance was placed "ahead" of a considerable portion of the arterial compliance. The plots which he obtained under these three conditions are in excellent qualitative agreement with the theoretical curves shown in Fig. 18, in which blood volume was varied from 2000 to 8000 cc with "normal" R_S and R_P, double R_S, and double R_P. We regard this agreement as additional evidence for the probable faithfulness of our model.

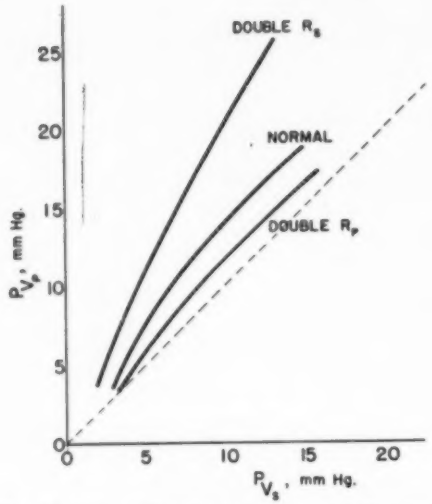

FIG. 18. P_{V_P} AS A FUNCTION OF P_{V_S} DURING CHANGES IN BLOOD VOLUME WHEN R_S AND R_P ARE NORMAL, WHEN R_S IS DOUBLED, AND WHEN R_P IS DOUBLED—THEORY

4. *Cardiac Frequency Changes.* This is one of the most interesting and complex forcings. In general, as mentioned previously, the "optimum frequency," F_o, for maximizing cardiac output will not be identical for the two ventricles. The predicted behavior of our model is shown in Fig. 19. As F increases from 40 to 80 cpm, the output of each ventricle increases. However, $(\partial Q_L/\partial F)_P < (\partial Q_R/\partial F)_P$ so that blood is transferred from systemic to pulmonary circuits to attain a steady state. As F rises from 80 to 120, these two rates of change become nearly identical, so that little transfer of blood between circuits occurs. Finally, as F increases above 120 cpm, blood begins to be transferred from pulmonary back to systemic circuit. Cardiac output, P_{A_S}, P_{A_P}, and P_{V_P} all have a maximum at about 120 cpm, while P_{V_S} has a minimum at this point. The fact that ventricular diastolic volumes go through a maximum at $F = 60$ is of interest. A large v_d is favored by (1) a low ratio, S/P_A (2) a long filling time, and (3) a high P_V. When F falls below 60, the rise in S_L/P_{A_S} and fall in P_{V_P} outweighs the influence of a longer

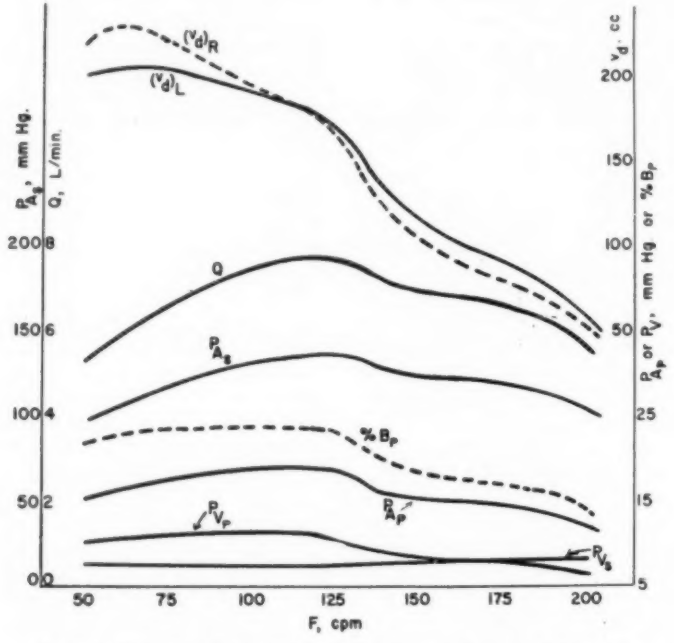

FIG. 19. THEORETICAL RESPONSES TO CHANGES IN CARDIAC FREQUENCY

filling time, so $(v_d)_L$ falls. On the right side, the rise in S_R/P_{AS} overbalances the increase in P_{VS} and filling time.

Unfortunately, detailed experimental data for comparison with these predictions are unavailable. In the "isolated heart" preparation of Katz, Wise, and Jochim (1945a,b), (a modified open-circuit heart-lung preparation), it has been shown that Q does go through a maximum as F is progressively increased, and that this change in Q is paralleled by changes in P_{AS} and P_{AP}, which is in agreement with the theory. However, these workers did not make a detailed study of frequency changes in their closed-circuit heart-lung preparation, so that the predicted intercircuit blood redistribution and the accompanying changes in P_{VS} and P_{VP} (which are critically dependent on system properties) cannot be checked at this time. Such a study would be highly desirable.

5. *Myocardial "Weakness"*. Fig. 20 shows the behavior of the model when the "strength" of the left (Fig. 20, left) or right (Fig. 20, right) ventricle is reduced from normal to 10 per cent of normal. When one or the other ventricle weakens, Q falls; blood accumulates in the circuit "behind" the weak pump; and the diastolic volume of the latter increases while that of the normal pump falls. Venous pressure rise "behind" the weak pump and falls "behind" the normal one. Although systemic arterial pressure falls when either ventricle weakens, pulmonary arterial pressure falls when the right pump is weak but rises when the left pump is weak. The absence of arterial "back pressure" in right weakness and its presence in left weakness is a consequence of the large ratio of systemic to pulmonary circuit compliance. Within limits, we can restore the cardiac output to normal by increasing the blood volume, and when we do this, all circuit pressures increase as well.

These predictions of the theory are in excellent agreement with the observations of Starr and Rawson (1940) in a mechanical model, as well as with those of Katz, Wise, and Jochim (1945c) in the closed-circuit heart-lung preparation. Although we believe that the terms "forward failure" and "backward failure" should be discarded because of the

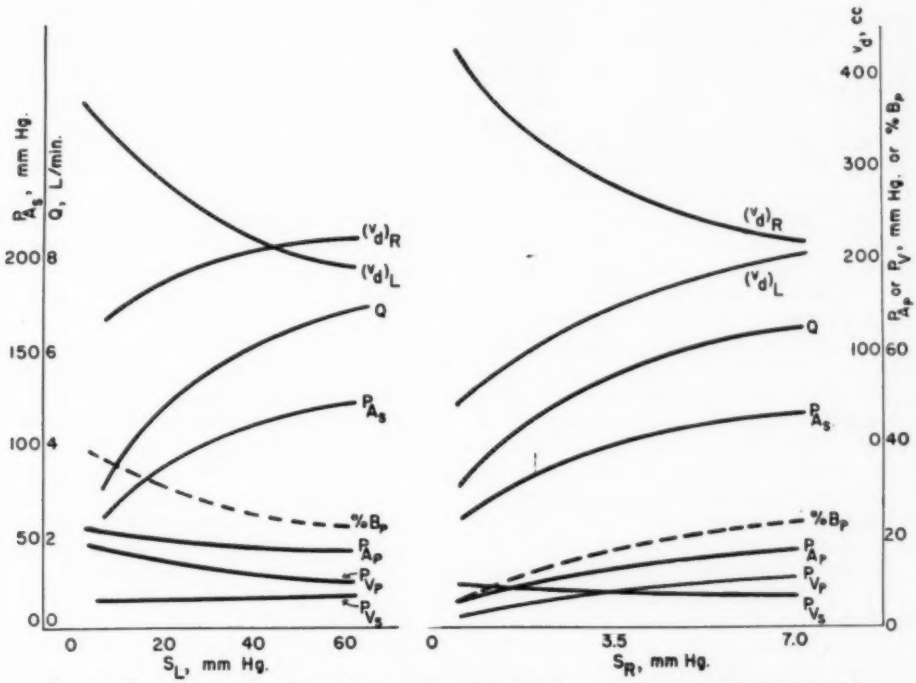

FIG. 20. THEORETICAL RESPONSES, LEFT, TO REDUCTION IN S_L, AND RIGHT, TO REDUCTION IN S_R

TABLE 2

Responses and Forcings in Exercise

RESPONSES	REST	EXERCISE	FORCINGS	REST	EXERCISE
Q, L/min	6.5	27	F, cpm	75	150
v_s, cc	86.6	180	S_L, mm Hg	50	135
$(w_s)_L$, g m	137	368	S_R, mm Hg	7	22.5
$(w_s)_R$, g m	20.8	61.5	R_LC_L, sec	0.35	0.09
$(v_d)_L$, cc	201	200	R_RC_R,* sec	0.35	0.28
$(v_d)_R$, cc	216	200	R_S, mm Hg/cc/min	0.0167	0.0053
$(v_r)_L$, cc	114	20	R_P, mm Hg/cc/min	0.001	0.00052
$(v_r)_R$, cc	114	20	C_{VS}, cc/mm Hg	500	490
P_{AS}, mm Hg	116	150			
P_{AP}, mm Hg	17.5	25			
P_{VS}, mm Hg	7.5	7.5			
P_{VP}, mm Hg	11.0	11.0			

* C_L and C_R constant

widespread ambiguity in their usage, we can point out that in the terminology used by Katz, Wies, and Jochim (1945c), the behavior illustrated in Fig. 20 would be called "mixed failure" because both a reduction in Q ("forward failure") and a rise in P_V behind the weak chamber ("backward" failure) occur simultaneously. If we define "failure" as a pure reduction in S_L or S_R with all other system properties constant, it is obvious that such failure must always be "mixed," as Fig. 20 illustrates.

6. *Normal Exercise. Combined Heart and Circuit Forcing.* Exercise places the most severe physiological demand upon the cardiovascular system. Cardiac output rises to four or five times its resting value as both frequency and stroke volume increase. Mean systemic arterial pressure rises, but very modestly compared to the change in cardiac output. Pulmonary arterial mean pressure rises very little (Riley, Himmelstein, Motley, Weiner, and Cournand, 1948). Despite an increase in ventricular stroke work, there appears to be no remarkable change either in diastolic volume or venous filling pressure (Rushmer, 1955; Liljestrand, Lysholm, and Nylin, 1938; Landis, Brown, Fanteux, and Wise, 1946). Prevalent misquotations to the contrary (Rushmer, 1955, 1956), this does not contradict Starling's position (Starling, 1918).

We may now ask how our model can reproduce this state of operation. We note first that neither cardiac forcing alone nor circuit forcing alone can do so. A combination of both is required. In Table 2 we have listed on the left side values for the dependent variables during normal rest and during an assumed state of vigorous exercise. On the right are listed the corresponding values for those independent variables whose manipulation is assumed to produce the exercise response. The cardiac forcing facilitates both filling (reduced RC) and emptying (increased S) of the ventricle. The circuit forcing prevents an excessive rise in arterial load pressures, as well as a fall in venous filling pressures. Note that we have said nothing about how these manipulations are accomplished but only that if they are, the observed behavior of the system in exercise can be reproduced. The "how" of the manipulation process of course involves the operation of the tissue gas exchanger as well as the neuro-humoral *controlling* system, which we shall not consider at this time. Mechanical non-linearity of R_P is also apparently involved.

DISCUSSION

Although it has been realized for many years that the cardiovascular system is a complex multivariate feedback regulator, a comprehensive analytical treatment of this system has not previously been attempted. It is not difficult to understand why. The very complexity of the system discourages such analysis on the one hand while simultaneously demanding it for adequate understanding on the other. In our initial effort, we attacked only a very limited objective—the isolated mechanical section of the controlled system. Even here many simplifying assumptions were introduced to facilitate the analysis. It was believed that an explicit identification of dependent and independent variables and of the relationships between them might

prove of value even though some of the functions used to specify these relationships were obvious approximations. The mathematical model so derived appeared capable of accounting reasonably well for a variety of experimental observations, and so we conclude that it is probably a faithful one. However, since its implications are so numerous, most of them remain to be checked against types of experimental data not now available. Such data are obviously not easy to obtain in a system involving such a large number of both dependent and independent variables, many of which are extremely difficult to measure or control. But it is in just such a system as this that a mathematical guide to investigation and understanding is indispensable. One must first know how the system should behave under any given set of premises before he can get very far in testing their adequacy.

Much of the current controversy concerning cardiac output regulation has centered around what is termed "the validity of Starling's law in the intact animal" (Stead and Warren, 1947; Sarnoff, 1955; Rushmer, 1955; Richards, 1955; Hamilton, 1955). Let us attempt to clarify this issue by asking two questions:

(1) Is ventricular stroke work a function of ventricular diastolic volume in the intact animal *provided cardiac properties remain constant*? This has been answered in the affirmative by Wiggers (Wiggers and Katz, 1922), Sarnoff (Sarnoff and Berglund, 1954); and others. Since this is all that Starling's law requires, we conclude that it "holds in the intact animal," a conclusion which is hardly surprising. [We need not be concerned with the statement of the law in terms of "total energy output" or oxygen consumption (Starling and Visscher, 1926–27)]. The fact that cardiac output is not a single valued function of "central venous pressure" in an intact animal in which both cardiac and circuit properties vary in uncontrolled fashion is irrelevant to this question (Stead and Warren, 1947), as is clearly brought out by both our mathematical and Sarnoff's experimental analyses (Sarnoff and Berglund, 1954).

(2) Are physiological changes in cardiac output brought about in the intact animal by cardiac forcings, circuit forcings, or both? This is a question of fundamental significance, but its nature has been obscured by confusing it with inquiries about the "validity of Starling's law" (Rushmer, 1955; Richards, 1955; Hamilton, 1955). Since we have already concluded above that "Starling's law holds in the intact animal," the answer to the present question cannot alter this conclusion. We are certain that those who claim that the physiological manipulation of ventricular strength in the intact animal invalidates Starling's law would not think of claiming that the physiological manipulation of peripheral resistance invalidates Poiseiulle's law (or its non-linear equivalent), or that the manual manipulation of a rheostat to regulate current flow in an electrical circuit invalidates Ohm's law! How then did this confusion arise? Doubtless because Starling's early papers overemphasized circuit forcings (or "venous return" in an often ambiguous terminology which we prefer to avoid) in the intact animal (Patterson and Starling, 1914). Over the course of time, this was distorted to imply that cardiac forcing and Starling's law were mutually exclusive. But Starling himself was under no such illusion. In his Linacre Lecture of 1915, he said that the heart was *not* dilated in the steady state of exercise in man because its "physiological condition" was improved, thus implying a shift to a new "Starling curve" (Sarnoff and Berglund, 1945). True, he attributed this improvement to an increased coronary flow rather than to the neural and humoral operations which we like to assume today; but he clearly recognized that both cardiac and circuit forcings operated in the intact animal, that myocardial strength (or "physiological condition") was not an invariant, and that such invariance, though necessary for the demonstration of his law, was not necessary for its validity (Patterson, Piper, and Starling, 1914; Starling, 1918). Much of the recent work in this field has consisted of a rediscovery of these concepts (Sarnoff, 1955; Rushmer, 1955a,b, 1956).

We implied above that we preferred to avoid the term "venous return" because it is shrouded in ambiguity and has generated endless confusion about cardiac output regulation. If we define "venous return" as the mean volume flow rate of blood entering either ventricle, "cardiac output" as the mean volume flow rate of blood leaving either ventricle, and restrict ourselves to steady-state operation, then the only meaningful statement we can make about these quantities is that "cardiac output equals venous return." This is simply a steady-state restriction free of all cause-effect implications. But we must not say (as is so commonly done) that "cardiac output is *determined* by venous return," for this statement might convince us that we have answered a significant question about cardiac out-

put regulation whereas in reality we have answered nothing at all! In the closed-circuit cardiovascular system, cardiac output and venous return are two points on the same moving circle. The motion of the circle, and thus of all of its points simultaneously, is determined by a combination of cardiac and circuit properties. This is one of the fundamental points which receives explicit clarification in our model.

In pursuing this study further, we shall try to advance along two fronts. First, we can assume that our present model is faithful enough to warrant its inclusion into more complex syntheses. Thus we can add a "tissue gas exchanger" and provide a "short" chemical loop whereby tissue (systemic venous) gas concentrations operate directly on R_S. Such a system would show a limited "self-regulation" of cardiac output in response to tissue metabolism. Instead of a single "lumped" exchanger, we could then introduce a number of parallel elements each with its own "short" chemical loop thus providing for a varied distribution of Q between a number of parallel systemic circuits. Our controlled system would then have two sorts of "short" feedback loops: (1) mechanical, through which circuit pressures influence cardiac output; and (2) chemical, through which tissue gas concentrations influence systemic arteriolar resistance. We call these "short" loops to indicate that they operate entirely within the controlled system. Finally, we could examine the operation of the neurohumoral controlling system and combine it with the controlled system. An obvious controlling operation for initial exploration would be the manipulation of F, S_L, S_R, R_S, and C_{VS} in response to P_{AS} levels monitored through the carotid sinus (a "long" feedback loop).

A second line of attack involves the refinement of our present model by introducing more complex functions which better approximate the physiological prototype. In this modern age of computers, such functions have become less forbidding. Thus, we can examine the modifications introduced by non-linear circuit properties, or more complex cardiac functions (Brecher, 1954; Brecher and Kessen, 1957). As a first step in this direction, we shall briefly examine some modified ventricular filling laws in Appendix 1.

But whatever modifications in detail our model may require in the future (and we know there will be many), we are confident that when a satisfactory understanding of cardiovascular regulation is finally attained, it will be expressed in the language and conform to the pattern which we have tried to use here. Perhaps the major contribution of the present analysis will be to assist in a more precise formulation of those questions whose answers will eventually lead to such understanding.

APPENDIX 1. ALTERNATIVE VENTRICULAR FILLING EQUATIONS

Although our model was reasonably successful in accounting for many aspects of over-all system behavior, there is an obvious detail which our ventricular filling law (equation 7) does not account for. This is the fact that during the early stages of ventricular filling, intraventricular pressure falls while ventricular volume is increasing (Wiggers, 1949). Our present model requires that both intraventricular pressure and ventricular volume rise together in parallel fashion from the moment filling begins. Let us now seek a modified filling law which can account for the observed behavior.

First we inquire whether the ventricular "suction" reported by Brecher (Brecher and Kessen, 1957) might be the answer. The negative (relative to ambient atmosphere) intraventricular pressures observed by Brecher appear to arise from the fact that the unstressed volume of the relaxed ventricle is somewhat greater than zero, and if the volume is reduced below this point, the wall develops a positive restoring force. [In the filling process, forces are considered positive if they drive filling.] A reasonable morphological basis for this has been identified by Rushmer (1955b). Let us take this into account while continuing to assume that the compliance of the relaxed ventricle is linear and that filling does not begin until relaxation is complete. This requires only a minor modification of equation (7):

$$RC\dot{v}_d + v_d = CP_V + v_0 \tag{65}$$

where v_0 is the unstressed volume. If $v_d = v_r$ at $t = 0$, the solution for v_d is:

$$v_d = (CP_V + v_0) + [v_r - (CP_V + v_0)]e^{-t/RC} \tag{66}$$

Considering the total viscance, R, to be composed of two series elements, R_1 ("bloodway viscance") and R_2 ("myocardial viscance"), the intraventricular pressure during filling, P_{IV}, is:

$$P_{IV} = P_V + (R_1/RC) \cdot [v_r - (CP_V + v_0)]e^{-t/RC} \tag{67}$$

Again, P_{IV} must rise exponentially from the moment filling begins. Beyond introducing the possibility of negative intraventricular pressures, we have produced no essential modification in our original model. Since there is every indication that v_0 is small and therefore usually less than v_r (Brecher and Kessen, 1957), we are content to omit this detail. It is worth noting that the presence of a myocardial viscance (R_2) makes intraventricular pressure an invalid index of ventricular volume under dynamic conditions. We conclude that "suction" alone cannot account for the fall in P_{IV} during early filling and that we must therefore look elsewhere.

Our previous assumption that ventricular relaxation is instantaneous is certainly unrealistic. If we abandon it, we must consider the possibility that filling may begin before relaxation is complete. During a finite relaxation period, any or all of the myocardial properties (v_0, C, R) may be time-dependent. The simplest possibility to explore is the one which assumes that both C and R instantaneously attain their final (relaxed) values but that v_0 requires a finite time to do so. Our differential equation for the filling process then becomes:

$$RC\dot{v}_d + v_d = CP_V + v_0(t) \tag{68}$$

where we have indicated that v_0 is now time-dependent. We define this dependence specifically as follows:

$$v_0(t) = v_{0_2} + (v_{0_1} - v_{0_2})e^{-t/k'} \tag{69}$$

where v_{0_1} is the value of v_0 at $t = 0$, v_{0_2} is the unstressed volume of the completely relaxed ventricle, and k' is the time constant for the relaxation process. Substituting equation (69) into (68):

$$RC\dot{v}_d + v_d = CP_V + v_{0_2} + (v_{0_1} - v_{0_2})e^{-t/k'} \tag{70}$$

taking $v_d = v_r$ at $t = 0$, the solution of equation (70) is:

$$v_d = [(v_{0_1} - v_{0_2})/[1 - (RC/k')]](e^{-t/k'} - e^{-t/RC}) + (v_r - CP_V - v_{0_2})e^{-t/RC} + CP_V + v_{0_2} \tag{71}$$

We still have a problem in the choice of v_{0_1}. If v_r is the volume of blood in the ventricle at the instant of semilunar valve closure, then we want $\dot{v}_d$ to be zero or positive (but never negative) from this instant forward during diastole. The period during which $\dot{v}_d = 0$ would correspond to "isometric relaxation," and $\dot{v}_d$ would become positive at the end of this period when the auriculo-ventricular (A-V) valve opened. Now equation (70) cannot describe isometric relaxation since it provides no A-V valve, and $\dot{v}_d$ would therefore be negative whenever $P_{IV} > P_V$. To avoid this difficulty, let us define the end of isometric relaxation as the instant, $t = 0$, and choose v_{0_1} in such a way that $\dot{v}_d = 0$ at this instant. This requires that:

$$P_{IV} = P_V \tag{72}$$

which will be true provided that

$$v_{0_1} = v_r - CP_V \tag{73}$$

Our problem is thus solved; but we must point out another apparent difficulty. If we deal with the left ventricle of the dog and take $C = 2.45$ cc/mm Hg and $P_V = 10$ mm Hg, equation (73) becomes:

$$v_{0_1} = v_r - 24.5 \tag{74}$$

and we see that v_{0_1} will be negative whenever $v_r < 24.5$ cc. Since this will usually be the case, we shall more often than not be using negative values for v_{0_1}. Now obviously these are virtual volumes which have no meaning in terms of actual physical volumes. Instead, we can interpret them in terms of "threshold" or "yield" pressures below which $v = 0$; and in this sense, we need not be disturbed by their use.

Incorporating restriction (73) in equation (71), we can finally write for ventricular volume:

$$v_d = [(v_r - CP_V - v_{0_2})/(1 - (RC/k'))](e^{-t/k'} - e^{-t/RC}) + (v_r - CP_V - v_{0_2})e^{-t/RC} + CP_V + v_{0_2} \tag{75}$$

The corresponding equation for intraventricular pressure is:

$$P_{IV} = P_V - R_1\{[(v_r - CP_V - v_{0_2})/(1 - (RC/k'))][(1/RC)e^{-t/RC} - (1/k')e^{-t/k'}] - (1/RC)(v_r - CP_V - v_{0_2})e^{-t/RC}\} \tag{76}$$

In the special case, $k' = RC$, the first term on the right in equation (75) assumes the indeterminate form, 0/0. Evaluation by L'Hospital's rule then yields:

$$v_d = (v_r - CP_V - v_{0_2})[(t/RC) + 1]e^{-t/RC} + CP_V + v_{0_2} \tag{77}$$

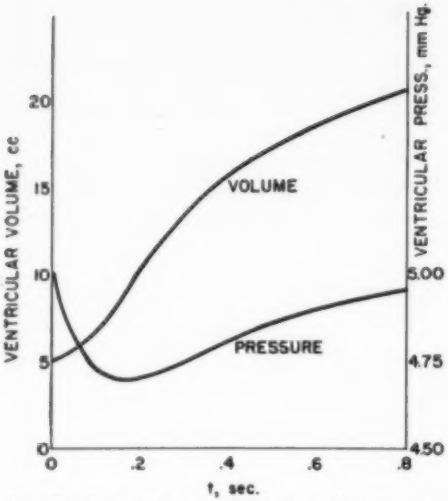

FIG. 21. BEHAVIOR OF VENTRICULAR VOLUME AND INTRAVENTRICULAR PRESSURE DURING FILLING WHEN v_o IS TIME-DEPENDENT

$$P_{IV} = P_V + R_1[t(v_r - CP_V - v_{0_2})/(RC)^2]e^{-t/RC} \quad (78)$$

In Fig. 21, we have plotted equations (75) and (76) using the following set of values for the constants: $k' = 0.1$ sec, $RC = 0.3$ sec, $v_r = 5$ cc, $v_{o_2} = 10$ cc, $C = 2.45$ cc/mm Hg, $P_V = 5$ mm Hg, and $R_1 = 0.009$ mm Hg/cc/sec. Both pressure and volume curves appear to agree well with observation (Wiggers, 1949). By adjusting the relative values of k', RC, and t, one can reproduce most varieties of pressure curves reported in the literature (Buckley, Sidkey, and Ogden, 1956; Wiggers, 1949; A. M. Katz, L. N. Katz, and Williams, 1955).

Of particular interest is the fact that the use of equation (75) instead of equation (8) to describe the filling process introduces no essential modification in the steady state behavior of the isolated ventricle. If we combine equation (75) with our "emptying equations," we get the following expression for cardiac output:

$$Q = FS(CP_V + v_{0_2})[(RC/k')e^{-t/RC} - e^{-t/k'} + 1 - (RC/k')]/[P_A(1 - (RC/k')) + (P_A - S)[(RC/k')e^{-t/RC} - e^{-t/k'}]] \quad (79)$$

where t is defined in terms of F by equation (9) as before. From equation (79), it is apparent that Q is a linear function of P_V and an hyperbolic function of P_A just as it was before (equation 16). We can also show that equation (79), like (16), defines an optimum frequency for maximum Q. Thus, if our primary concern is with over-all system behavior, we can continue to use the simpler form of equation (16).

Let us finally examine one other alternative. We return to our original assumption that $v_0 = 0$, but now permit C to vary as a function of time during diastole. The differential equation for filling then becomes:

$$RC(t)\dot{v}_d + v_d = C(t)P_V \quad (80)$$

and we now have the mathematically complex situation of "parametric forcing." Let us define the time dependence of C as:

$$C(t) = C_2 + (C_1 - C_2)e^{-t/k'} \quad (81)$$

where C_1 is the value of C at $t = 0$, C_2 is the compliance of the fully relaxed ventricle, and k' is the time constant for the relaxation process. Substituting equation (81) into equation (80) yields:

$$R[C_2 + (C_1 - C_2)e^{-t/k'}]\dot{v}_d + v_d = P_V[C_2 + (C_1 - C_2)e^{-t/k'}] \quad (82)$$

The general solution of equation (82) can be written as follows:

$$v_d = G_i(T_2 e^{t/k'} + A')^{-k'/T_2} + (P_V/R)(T_2 e^{t/k'} + A')^{-k'/T_2} \int (T_2 e^{t/k'} + A')^{k'/T_2} dt \quad (83)$$

where

$$T_2 \equiv RC_2 \quad (84)$$

$$A' \equiv R(C_1 - C_2) = T_1 - T_2 \quad (85)$$

and G_i is an arbitrary constant to be determined from an initial condition. The integral in equation (83) is readily evaluated for the special case:

$$k' = T_2 \quad (86)$$

and under these conditions, taking $v_d = v_r$ at $t = 0$, equation (83) becomes:

$$v_d = [(v_r T_1 - P_V C_2 T_2)/(T_2 e^{t/T_2} + A')] + [P_V(T_2^2 e^{t/T_2} + A't)/R(T_2 e^{t/T_2} + A')] \quad (87)$$

The corresponding equation for intraventricular pressure is:

$$P_{IV} = P_V - R_1\{(P_V/R)[1 - \{(T_2^2\, e^{t/T_2} + A't)e^{t/T_2}/(T_2\, e^{t/T_2} + A')^2\}] - (v_r T_1 - P_V C_2 T_2)\, e^{t/T_2}/(T_2\, e^{t/T_2} + A')^2\} \quad (88)$$

Again, for reasons explained above, we define the end of "isometric relaxation" as the instant $t = 0$ and choose T_1 such that:

$$T_1 = Rv_r/P_V \quad (89)$$

In Fig. 22, we have plotted equations (87) and (88) using values for the constants which might be appropriate for the human left ventricle: $P_V = 10$ mm Hg, $C_2 = 20$ cc/mm Hg, $R = 0.0175$ mm Hg/cc/sec, $R_1 = 0.0082$ mm Hg/cc/sec, $T_2 = RC_2 = 0.35$ sec, $v_r = 80$ cc, $T_1 = Rv_r/P_V = 0.14$ sec. Again both pressure and volume curves agree reasonably well with observation.

If we combine equation (87) with our "emptying equations" we get the following expression for cardiac output in the isolated ventricle:

$$Q = (FSP_V/RP_A)\{[-(T_2\, e^{t/T_2} - T_2 - Zt)/2Z(1 - Z)] + [[(T_2\, e^{t/T_2} - T_2 - Zt)/2Z(1 - Z)]^2 - (T_2^2 - T_2^2\, e^{t/T_2} + T_2 t)/Z(1 - Z)]^{1/2}\} \quad (90)$$

where:

$$Z = 1 - (S/P_A) \quad (91)$$

and t is defined in terms of F by equation (9), as before. Again we see that Q is a linear function of P_V in equation (90) just as it was in equations (79) and (16). However, Q is not a perfect hyperbolic function of P_A although it still decreases in curvilinear fashion, with concavity upward, as before. Also, equation (90) does not appear to define an optimum frequency for maximizing Q. Thus the steady-state behavior of the isolated ventricle predicted by equation (90) differs somewhat from that predicted by both equations (79) and (16). The latter two appear to be in better agreement with observation. We shall not explore the implications of a time-dependent compliance further at this time because of the difficulty in evaluating the integral in equation (83) for the general case, $k' \neq T_2$.

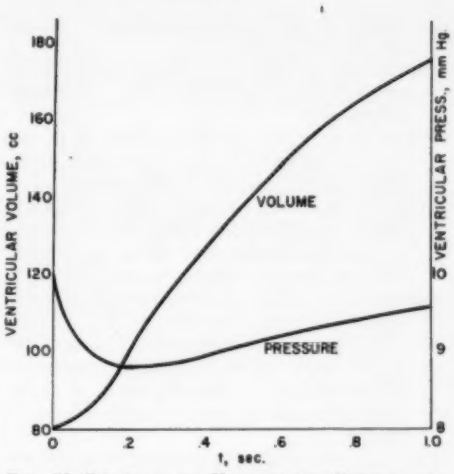

FIG. 22. BEHAVIOR OF VENTRICULAR VOLUME AND INTRAVENTRICULAR PRESSURE DURING FILLING WHEN C IS TIME-DEPENDENT

ACKNOWLEDGMENTS

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LIST OF LITERATURE

ANREP, G. V., and E. BULATAO. 1925. Observations on the pulmonary circulation. Pulmonary circulation in the heart-lung preparation. *J. Physiol.*, 60: 175–192.

BERGLUND, E. 1954. Ventricular function. VI. Balance of left and right ventricular output: relation between left and right atrial pressures. *Amer. J. Physiol.*, 178: 381–386.

BRECHER, G. A. 1954. Cardiac variations in venous return studied with a new bristle flowmeter. *Amer. J. Physiol.*, 176: 423–430.

——. 1956. *Venous Return*. 148 pp. Grune & Stratton, New York.

——, and A. T. KESSEN. 1957. Relation of negative intraventricular pressure to ventricular volume. *Circulation Res.*, 5: 157–162.

BUCKLEY, N. M., M. SIDKEY, and E. OGDEN. 1956. Factors altering the filling of the isolated left ventricle of the dog heart. *Circulation Res.*, 4: 148–156.

DALY, I. DE BURGH. 1925a. A closed circuit heart-lung preparation. I. Effects of alterations in blood volume. *J. Physiol.*, 60: 103–108.

——. 1925b. A closed circuit heart-lung preparation. Effect of alterations in the peripheral resistance

and in the capacity of the circulation. *Proc. roy. Soc., B*, 99: 306–325.

FÜHNER, H., and E. H. STARLING. 1913. Experiments on the pulmonary circulation. *J. Physiol.*, 47: 286–304.

GAUER, O. H. 1955. Volume changes of the left ventricle during blood pooling and exercise in the intact animal. *Physiol. Rev.*, 35: 143–155.

GREGG, D. E., D. C. SABISTON, and E. O. THEILIN. 1955. Changes in left ventricular end-diastolic pressure and stroke work during infusion and following exercise. *Physiol. Rev.*, 35: 130–136.

GRODINS, F. S. 1955. Theoretical analysis of cardiac output regulation. *Fed. Proc.*, 14: 64.

——, J. S. GRAY, K. R. SCHROEDER, A. L. NORINS, and R. W. JONES. 1954. Respiratory responses to CO_2 inhalation. A theoretical study of a nonlinear biological regulator. *J. appl. Physiol.*, 7: 283–308.

GUYTON, A. C. 1955. Determination of cardiac output by equating venous return curves with cardiac response curves. *Physiol. Rev.*, 35: 123–129.

HAMILTON, W. F. 1953. The physiology of the cardiac output. *Circulation*, 8: 527–543.

——. 1955. Role of Starling concept in regulation of normal circulation. *Physiol. Rev.*, 35: 161–168.

KATZ, A. M., L. N. KATZ, and F. L. WILLIAMS. 1955. Registration of left ventricular volume curves in the dog with the systemic circulation intact. *Circulation Res.*, 3: 588–593.

KATZ, L. N. 1955. Analysis of the several factors regulating the performance of the heart. *Physiol. Rev.*, 35: 91–106.

——, W. WISE, and K. JOCHIM. 1945a. Dynamics of the isolated heart and heart-lung preparation of the dog. *Amer. J. Physiol.*, 143: 463–478.

——, ——, and ——. 1945b. The dynamics of the non-failure period of the isolated heart and heart-lung preparation. *Amer. J. Physiol.*, 143: 495–506.

——, ——, and ——. 1945c. The dynamic alterations in heart-failure in the isolated heart and heart-lung preparation. *Amer. J. Physiol.*, 143: 507–520.

KUNO, Y. 1915. Contributions to the physiology of the pulmonary circulation. *J. Physiol.*, 50: 140–153.

LANDIS, E. M., E. BROWN, M. FANTEUX, and C. WISE. 1946. Central venous pressure in relation to cardiac competence, blood volume, and exercise. *J. clin. Invest.*, 25: 237–255.

LILJESTRAND, G., E. LYSHOLM, and G. NYLIN. 1938. The immediate effects of muscular work on the stroke and heart volumes in man. *Skand. Arch. Physiol.*, 80: 265–282.

MARKWALDER, J., and E. H. STARLING. 1914. On the constancy of the systolic output under varying conditions. *J. Physiol.*, 48: 348–356.

PATTERSON, S. W., and E. H. STARLING. 1914. On the mechanical factors which determine the output of the ventricles. *J. Physiol.*, 48: 357–379.

——, H. PIPER, and E. H. STARLING. 1914. The regulation of the heart beat. *J. Physiol.*, 48: 465–513.

RICHARDS, D. W. 1955. Discussion of Starling's Law of the Heart. *Physiol Rev.*, 35: 156–160.

RILEY, R. L., A. HIMMELSTEIN, H. L. MOTELY, H. M. WEINER, and A. COURNAND. 1948. Studies of the pulmonary circulation at rest and during exercise in normal individuals and in patients with chronic pulmonary disease. *Amer. J. Physiol.*, 152: 372–382.

RUSHMER, R. F. 1955a. Applicability of Starling's Law of the Heart to intact unanesthetized animals. *Physiol. Rev.*, 35: 138–142.

——. 1955b. *Cardiac Diagnosis*. 447 pp. W. B. Saunders Co., Philadelphia.

——. 1956. Anatomy and physiology of ventricular function. *Physiol. Rev.*, 36: 400–425.

SARNOFF, S. J. 1955. Myocardial contractility as described by ventricular function curves. *Physiol. Rev.*, 35: 107–122.

——, and E. BERGLUND. 1954. Ventricular function. I. Starling's law of the heart studied by means of simultaneous left and right ventricular function curves in the dog. *Circulation*, 9: 706–718.

STARLING, E. H. 1918. *The Linacre Lecture on the Law of the Heart*. 27 pp. Longmans, Green & Co., London.

——, and M. B. VISSCHER. 1926–27. The regulation of the energy output of the heart. *J. Physiol.*, 62: 243–261.

STARR, I., and A. J. RAWSON. 1940. Role of the "static blood pressure" in abnormal increments of venous pressure especially in heart failure. I. Theoretical studies on an improved circulation schema whose pumps obey Starling's law of the heart. *Amer. J. Med. Sci.*, 199: 27–39.

STEAD, E. A., and J. V. WARREN. 1947. Cardiac output in man. *Arch. int. Med.*, 80: 237–248.

WEBER, E. H. 1850. *Ber. sächs. Ges. (Akad.) Wiss.*, 196.

WIGGERS, C. J. 1921a. The regulation of the pulmonary circulation. *Physiol. Rev.*, 1: 239–268.

——. 1921b. The present status of cardiodynamic studies on normal and pathologic hearts. *Arch. int. Med.* 27: 475–502.

——. 1949. *Physiology in Health and Disease*. 1242 pp. Lea & Febiger, Philadelphia.

——, and L. N. KATZ. 1922. The contour of the ventricular volume curves under different conditions. *Amer. J. Physiol.*, 58: 439–475.

ORIGIN AND COMPARISON OF THE EFFECTS OF TIME AND HIGH-ENERGY RADIATIONS ON LIVING SYSTEMS

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ABSTRACT

The process of aging may be regarded as the totality of those changes in structure, and consequently in function, which take place after reproductive maturity and which result in decreased adaptation to the environment. Built into the design and structure of an organism, this process is reflected in an increased probability of death. The well-known Gompertz equation describing increasing mortality with age has given rise to a number of theories which are shown to be, in one or more points, inadequate and inconsistent with established data.—All changes affecting the fitness of organisms are basically changes in the kinds, amounts, or arrangements of molecules and cells. Changes with age arise either from stochastic changes or from genetic processes, and should satisfy four criteria: universality, intrinsicality, progessiveness, and deleteriousness. The evolutionary origin of the aging process and the nature of the possible sources of instability afford evidence that there are multiple causes of aging. It is not at present possible to assign relative weights to the various processes.—The current thesis that the life-shortening of experimental animals exposed to ionizing radiation is attributable to an acceleration of the normal aging process is evaluated in terms of the sources and mechanisms of damage. It is concluded that time and radiation are unlikely to produce their de-adaptive effects by similar mechanisms because (1) aging is primarily an effect on postmitotic cells, whereas at low dosages radiation primarily affects dividing cell lines; (2) radiation damage is primarily genetic, whereas time produces many kinds of changes most of which are probably not genetic; (3) the lives of some experimental animals are not shortened by large doses of radiation; and (4) radiation dosages sufficient to double the rate of mortality increase produce a much greater than two-fold increase in genetic effects (mutation).

INTRODUCTION

During recent years, work in a number of laboratories (Henshaw, Stapleton, and Riley, 1947; Furth, Upton, Christenberry, Benedict, and Moshman, 1954; Brues and Sacher, 1952; Curtis and Healy, 1958; Casarett, 1959) has established the fact that animals exposed to moderate doses of ionizing radiation suffer from a decreased life expectancy, among other things. The incidence of specific diseases, especially cancer and leukemia, is known to increase as a result of this exposure. But, in addition, it has been suggested that the increased mortality may be due to a general acceleration of the "normal aging process" by ionizing radiation.

While it does not appear reasonable a priori to equate such incompletely understood and complex phenomena as radiation damage and aging, the idea has attracted sufficient attention that an analysis of the pros and cons of the theory in the light of research on aging may be instructive. In this paper the aging of biological systems will be defined in several contexts. A categorical analysis of the kinds of events which are considered to lead to age changes and a state-

ment of some criteria for biological aging will be made. A critical review of the appropriateness of known radiation effects, both qualitatively and quantitatively, as agents possibly responsible for "accelerated aging" will be undertaken. Briefly, it is concluded that certain effects of radiation are similar to, and perhaps identical with, some of the processes responsible for normal aging. But it is also concluded that the general thesis that radiation life-shortening mimics in detail the effects of time is inconsistent with certain experimental observations.

DEFINITIONS

Aging. Biological aging is here defined as the gradual decrease in an organism's adaptation to its normal environment following the onset of reproductive maturity (see also Medawar, 1951, and Comfort, 1956). This decreased adaptation expresses itself in a decreased capacity of the individual organism to carry out various specialized functions. The over-all effect of this functional decrement is an increased probability of death with the passage of time.

Specifically excluded from this definition of aging are diseases and pathological processes which are not universally encountered in the very old members of a species. Thus, while aging animals may exhibit (and do exhibit) a great increase in the frequency of specific diseases and pathological processes, such increased disease incidences are viewed as side effects of aging or of other underlying processes rather than as central causative agents of aging.

Disease. For the purposes of this discussion, diseases (pathological processes) are considered to be specific types of dysfunction caused by internal (e.g., genetic defects) or environmental factors which are not, however, universal in their occurrence in the very old animals of a species.

MEASUREMENT OF AGING

The physiological age and the chronological age of an animal may be quite different, but there is, at present, no reliable series of objective criteria of the rate of aging or of the physiological age of an animal. Ideally, it would be desirable to assess an animal's physiological age through a series of measurements of structure and tests of performance. Implicit in the measurement of various physiological capacities of animals and human beings of known age being conducted in the Gerontology Branch, National Heart Institute, and the Baltimore City Hospitals is an attempt to assess on the basis of physiological performance the chronological age of an animal (Davies and Shock, 1950; Norris, Shock, and Wagman, 1953; Shock and Yiengst, 1952; Landowne et al., 1955; Falzone and Shock, 1956; Shock, 1957). However, because of the considerable scatter of values of various physiological capacities from individual to individual, such measurements may, in general, be less valid than the purely subjective estimates of chronological age which the practiced observer can make. Many individuals have, however, pointed out that the rate of aging of populations of animals may be deduced from a comparison of the mortality rate and calendar age.

Among the most interesting of the mathematical relationships induced from the study of mortality rates versus age is the relationship first described by Gompertz in 1825 ($R = R_0 e^{\alpha t}$). Gompertz showed that the death rate increases logarithmically in most human populations between the ages of approximately 30 and 85 years. A similar logarithmic relationship is also true for a number of animal species. The constant (α) in the Gompertz equation has been considered to be an index of the *rate* of aging. For different animal species (Pearl and Miner, 1935), the time required for the mortality rate to double varies quite widely, from a few days in the case of *Drosophila* to about 8 years in the case of the human (Fig. 1). This Gompertz relationship is one of the most carefully measured of biological phenomena and, at the same time, most firmly established characteristics of the aging process in many populations.

Because of the fact that a number of analyses of the effects of radiation on aging deal with the Gompertz function and also because of the fact that any future theories, which may attempt to deal with the nature of aging or the effects of radiation, should also take into account the Gompertz relationship, we will here briefly review various of the theories which have been set forth to explain the form of the equation. Brody, in 1923, basing his theory on the change in various physiological parameters, notably milk production (which decays according to a simple first-order exponential), and recently Failla (1958, 1959a), who argues from first principles of physics and radiobiology, have alike set forth the concept

of vitality which behaves according to the same exponential decay law. Now, if one makes the assumption that the probability of death is inversely proportional to the vitality, it can be seen that the probability of death will increase as a first-order exponential function.

Brody Theory:

V = vitality
V_o = hypothetical vitality at zero time
$V \sim$ function (such as milk production) of performance
Assume that

(1) $V = V_o e^{-\alpha t}$ where α is the rate constant for the loss of function and the mortality rate R varies as $1/V$

(2) That is, $R = k \cdot (1/V)$

Substituting in (1),

(3) we obtain $R = k \cdot \frac{1}{V_o} e^{-\alpha t} = \frac{k}{V_o} e^{\alpha t}$

(4) Then defining $R_o = (k/V_o)$

(5) We obtain $R = R_o e^{\alpha t}$ (Gompertz equation)
By contrast, Failla takes the observed equation and argues from it by the approximate reverse of the above that a single-hit first order decay is involved through a mutation process.

The chief difficulty with these theories is that they imply that the vitality decreases by nearly a factor of 1,000 between the ages of 20 and 90 (because the mortality rate increases by approximately a factor of 1,000). Such a drastic change in any of the physiological capacities of the human organism essential to its survival is in conflict with the measured performance capacities of normal aged and young human beings (see Shock, 1957) and also with an intuitive estimate of the percentage loss of functional capacity in the aged.

Jones (1956a, b), starting with entirely different basic assumptions and with the observation that the incidences of various pathological conditions are positively correlated at any age, has suggested a theory of aging and mortality which is based upon the assumption that early disease and pathology make the organism susceptible to further disease. Jones assumes that the death rate is proportional to the accumulated amount of damage, and that the rate of accumulation of damage is proportional to the amount of damage

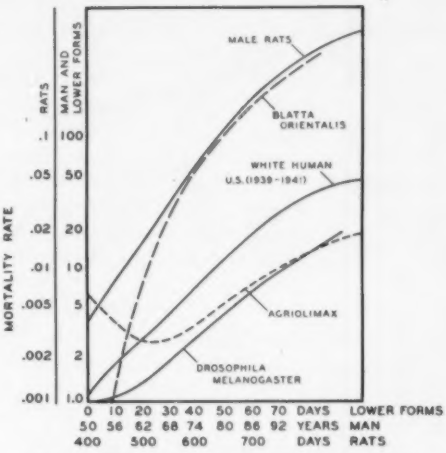


FIG. 1. GOMPERTZ PLOT OF THE RELATIONSHIP BETWEEN AGE AND MORTALITY RATE FOR A NUMBER OF SPECIES

Data from Pearl and Miner (1935) and Lansing (1952). Wild type *D. melanogaster* exhibits a strikingly linear relationship between age and log mortality rate over several log units, as do nearly all human beings residing in civilized environments. (See U. N. Yearbook, 1955).

which has already been accumulated. Disease and pathology are thus viewed as autocatalytic parasites upon the individual organism. Certain diseases undoubtedly leave a lasting imprint upon an organism which may weaken him when faced with other disease entities. But, on the basis of the recent experiments of Curtis and Healy (1958), it does not seem likely that this mechanism is generally operative in such experimental animals as the mouse. These authors have shown that exposure of experimental animals to toxic substances (e.g., diphtheria toxin) sufficient to kill a substantial fraction of them does not appreciably affect the life span of those animals which survived the acute effects of the exposure. Although there is evidence that the rate at which new pathological conditions make their appearance in a population of animals increases logarithmically, there is no evidence that the accumulated pathology in individual animals undergoes any such autocatalytic growth, since the time required for a disease to run its course is independent of age (Simms and Berg, 1958). Rather, if one accepts the measures of physiological function versus age which Shock and colleagues have collected, one can see that there is

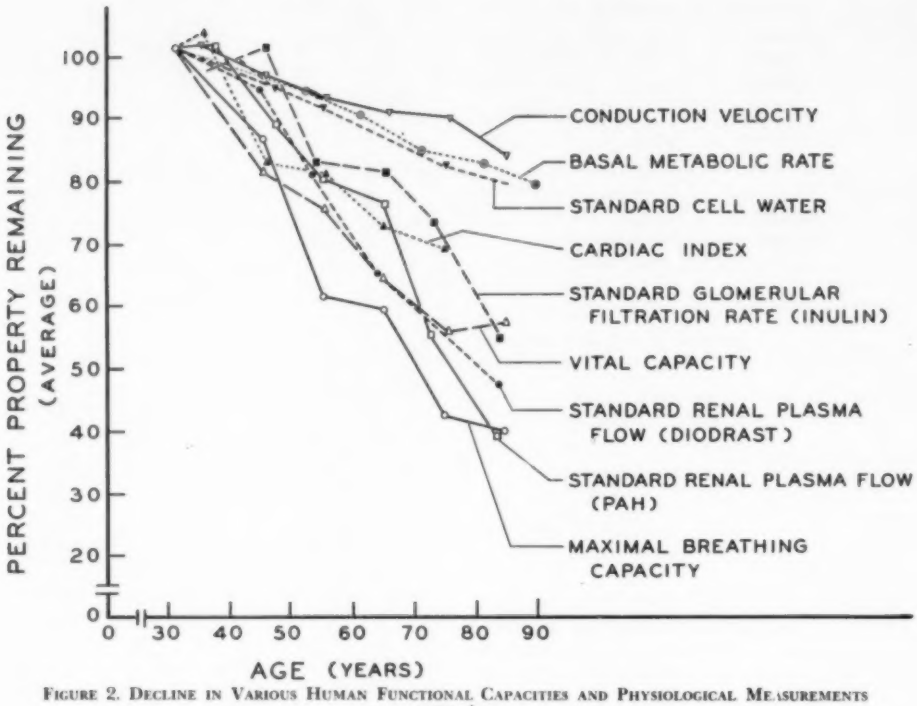


FIGURE 2. DECLINE IN VARIOUS HUMAN FUNCTIONAL CAPACITIES AND PHYSIOLOGICAL MEASUREMENTS WITH AGE

See text for explanation. Values are adjusted so that the value at age 30 equals 100 per cent. Other values are expressed as the average percentage of the value at age 30 remaining at the specified age.

no evidence of an increasing rate of accumulation of damage with advancing age. The decrement in physiological capacity is of the order of 5 to 13 per cent per decade, and the regression line is fitted as well by a straight line as by any other function (Fig. 2).

In devising his theory, Jones has also used the fact that human populations that show a low disease incidence during childhood also show a low incidence at later stages in the life span, while the opposite is true of populations showing a high incidence of disease during early years. His theory predicts such a relationship. But it should be pointed out that the probability of disease and death depends principally upon environmental conditions, and particularly on the indirect influence of civilization on medical care and public health practices. Since environmental changes will affect the mortality rate of both young and old individuals, the gradual improvement in mortality behavior at all ages is to be expected. This correlation is thus not a valid test of Jones' theory.

Two recent theories of mortality which attempt to account for the Gompertz equation and which have certain elements in common are those proposed respectively by Sacher (1956), and by Strehler (1959a) and Strehler and Mildvan (1959). In contrast to the theories mentioned earlier, these consider death at any age to be an improbable event which occurs when the organism's capacity to restore a stable condition is exceeded by a relatively rare internal or external disturbance of considerable magnitude. The theories differ from each other, however, in that the former relies principally upon a Gaussian distribution of internal fluctuations of homeostatic mechanisms about some mean value (which mean, in turn, decreases linearly with time).

Sacher Theory:

A. Sacher assumes that the various homeostatic mechanisms maintaining the integrity of an organism undergo displacements or fluctuations about the means which are Gaussian, thus:

(1) $P(u) = (2\pi\sigma^2)^{-1/2}\, e^{-u^2/2\sigma^2}$

where $P(u)$ = probability of finding a particular value differing from the mean (m) by a value u at time t and σ^2 is related to the mean value of the fluctuations.

B. If individuals are removed from the population when a fluctuation exceeds a limiting value L, where $\lambda = L - m$ the distribution approximates:

(2) $Q(u) = (2\pi\sigma^2)^{-1/2}\, e^{-u2/2\sigma^2} - e^{-(2\lambda-u)^2/2\sigma^2}$

C. When the reserve is large compared to the average fluctuations (that is, if $\lambda \gg 2\sigma$) it can be shown that

(3) $p = \frac{g\lambda}{\sigma}\left(\frac{2}{\pi}\right)^{1/2} e^{-\lambda^2/2\sigma^2}$

(4) But, by definition $\lambda = \lambda_o - \Delta\lambda$

(5) and $\lambda^2 = \lambda_o^2 - 2\lambda_o\Delta\lambda + \Delta\lambda^2$ so that

(6) $\lambda^2 = \lambda_o^2 - 2\lambda_o\Delta\lambda$ if and only if $\Delta\lambda/\lambda$ is very small.

(7) Under these conditions $\lambda \cong \lambda_o$; that is, the percentage change in reserve is very small, since $\Delta\lambda \to 0$.

Now, by substitution of (6) and (7) in (3) we obtain

$$p = \frac{g\lambda_0}{\sigma}\left(\frac{2}{\pi}\right)^{1/2} e^{-(\lambda_0^2 - 2\gamma_0\Delta\lambda)/2\sigma^2}$$

(8) $= K(\lambda_o/\sigma)\, e^{-\lambda_0^2/2\sigma^2}\ e^{\lambda_0\Delta\lambda/\sigma^2}$

Now $\Delta\lambda = \lambda_o\beta t$ if the mean decreases at a constant rate, so that

(9) p = Rate

$= K(\lambda_o/\sigma)\, e^{-\lambda_0^2/2\sigma^2}\ e^{\lambda_0\lambda_0\beta t/\sigma^2}$

α = observed Gompertz slope

$= (\lambda_o^2\beta/\sigma^2)$ or $(\alpha/\beta) = (\lambda_o^2/\sigma^2)$

(10) Therefore $R = K\sqrt{(\alpha/\beta)}\, e^{-(\alpha/2\beta)}\, e^{\alpha t}$

(11) and $R_o = K\sqrt{(\alpha/\beta)}\, e^{-(\alpha/2\beta)}$

(12) Substituting (11) in (10), we obtain $R = R_o\, e^{\alpha t}$, the Gompertz equation.

The second theory mentioned postulates that the Gompertzian increase in probability of death is a consequence of the interaction of (1) a linear decrease in the size of the maximum stress which the system can resist, and (2) a distribution of stresses which increases logarithmically in number as the magnitude of the stresses decreases. Such a distribution is analogous to the Maxwell-Boltzmann distribution of kinetic energies of molecules in a gas (see Getman and Daniels, 1943). By analogy, similar kinetics to the kinetics of death would be given by a chemical reaction which undergoes a linear decrease in activation energy with the passage of time.

Strehler Theory:

A. Assumes that the ability to resist agents which could produce death decreases linearly with time; that is, V = vitality = ability to resist disturbances, challenges, stresses, etc.

(1) $V_o - \beta t V_0 = V_0(1 - \beta t)$

where V_0 = hypothetical reserve capacity at zero time,
where β = rate constant for fraction of V lost per unit time, and where t = age or time.

B. Assume that the events which challenge an organism are disturbances in the energetic environment or internal environment, and that there is an exponentially decreasing probability of encountering events as their magnitude increases linearly. Distributions of this sort exist in nature and are particularly well documented at the molecular level, where, for example, the Maxwell-Boltzmann distribution when $E \gg RT$ is:

(2) $\frac{n}{n_t} = \frac{2}{\pi}\left(\frac{E}{R_t}\right)^{1/2} e^{-E/RT}$

(3) $R = k(n/nt) \cong C_0\, e^{-E/RT}$, since $\sqrt{(E/RT)}$ changes slowly compared to the exponential term. That is, the fraction of molecules having an energy equal to or greater than E decreases exponentially as E increases linearly. If we substitute V for E and take RT to be a measure of the poorness of an environment, we obtain

(4) $\frac{n}{n_t} = R = C_0\, e^{-E/RT} = C_0\, e^{-V/RT}$

$= C_0\, e^{-V_0(1-\beta t))/RT}$

or

(5) $R = C_0\, e^{-V_0/RT}\ e^{+V_0\beta t/RT}$. Define $R_0 = C_0\, e^{-V_0/RT}$ and $\alpha = V_0\beta/RT$, and we obtain

(6) $R = R_0\, e^{\alpha t}$ which is, again, the Gompertz equation.

C. The model can readily be adapted to radiation effects. Thus, if we assume that radiation damage is proportional to accumulated dose, and if vitality decreases proportional to the damage, we have the following:

(7) $V = V_0 - V_0\beta t - V_0 R_t\gamma$ (where R_t is the total radiation dose (roentgens) and γ represents the effectiveness per roentgen)

(8) or $V = V_0(1 - \beta t - R_t\gamma)$

(9) but $R_t = rt$ where r is dose rate and t is time of dose.

(10) Substituting $V = V_0(1 - \beta t - rt\gamma)$

$$= V_0(1 - (\beta + \gamma r)t)$$

and from equation (4)

$$\frac{n}{n_t} = R = C_0\, e^{-V_0[1-(\beta+\gamma r)t]/RT}$$

$$= C_0\, e^{-(V_0/RT)}\, e^{(\beta+\gamma r)t}$$

$$= R_0\, e^{(\beta+\gamma r)t}$$

The model thus is consistent with the observed effectiveness of radiation in increasing the Gompertz slope proportional to r. (Fig. 3).

Yockey (1958) and Szilard (1959) have also recently published theories of aging and mortality based on genetic premises. Yockey's theory is built upon the assumption that an organism dies when the amount of information loss as a result of the passage of time, exposure to radiation, or other disruptive factors reaches a critical value. He has analyzed the survivorship curves of a number of species and has compared them with single and multiple hit survivorship curves such as have been obtained with simple unicellular organisms (see Hollaender and Claus, 1936). For species that do not exhibit aging or, at least, which do not generally die of old age, the parallelism to bacterial survival curves is reasonably close (see also Comfort, 1956). However, Yockey's theory does not make any predictions regarding the relationship of metazoan survivorship or mortality to age. It particularly does not deal with the striking Gompertz relationship. Since the theory must assume ad hoc a very special function relating time and the decrease of information in a Gompertzian population (i.e., one displaying the Gompertz relationship), it is not sufficiently predictive to be subjected to the critical tests by which the above theories may be analyzed.

Szilard's theory represents an attempt to account for the distribution of ages at death on the basis of (a) an initial distribution of genetic variability in a population; (b) some rate of accumulation of hits, "faults," or damage to the genetic material; and (c) the occurrence of death when the accumulated faults reach a critical

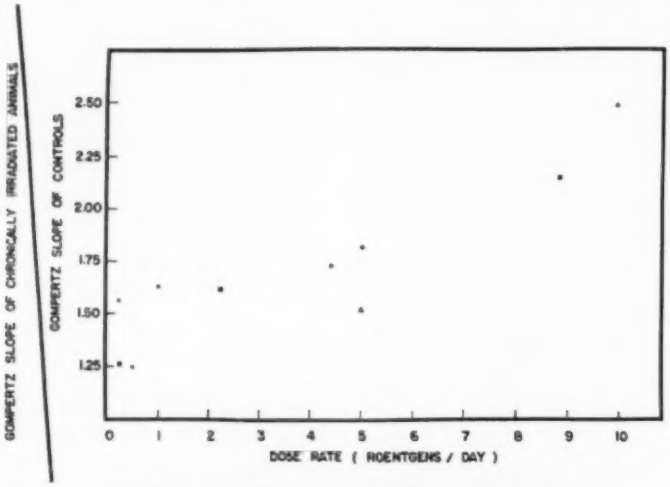


FIG. 3. EFFECT OF DOSE RATE ON THE GOMPERTZ SLOPE

Data abstracted from Berlin and DiMaggio (1956). The Gompertz slope is expressed as the slope for unirradiated controls divided into the slope characteristic of irradiated animals.

threshold level. The theory is not stated in a form which enables it to be compared directly with the other theories and observations, particularly the Gompertz relationship. Moreover, it must assume a particular ad hoc distribution of initial faults in order to account for observed age-specific death rates or, alternatively, the distribution of ages at death. Szilard does not evaluate the goodness of fit of the theory to mortality data, nor does he give the theoretical basis for the kind of distribution he chooses. For this reason, a final critical analysis of his theory, like Yockey's, appears to await a more definite and detailed statement of its underlying postulates. A critical analysis and evaluation of various mathematical theories of mortality and aging will appear elsewhere in the near future (Mildvan and Strehler, 1959).

GENERAL CATEGORIES OF AGE CHANGES

Many possible classifications of the kinds of changes leading to decreased functional capacity of old animals are possible. For the purposes of this discussion, however, it may be useful to divide the types of processes which can lead to decreased function into two categories: those which we shall call determinate processes, and those which may be termed ancillary processes. Determinate processes are such processes as are certain to occur in all animals of a given kind regardless of their environment and experience. (By the earlier definition this includes "normal aging.") Such processes can be considered to be a consequence of (a) the finite stability of any machine (Eden, 1956); (b) the probability that any machine will make errors in its normal functions (Yockey, 1956); (c) the fact that evolutionary selection may largely ignore the debilities of old age (Medawar, 1951); or (d) even, as has been suggested by Weismann (1882), Medawar (1951), and Williams (1957), built-in factors (genes or gene combinations) which lead to an increased survival capacity at an early age but which produce a decreased survival capacity later, etc.

Ancillary processes leading to decreased performance of old organisms, on the other hand, may be considered as the consequences of gross accidental events which are not predictable on the basis of the structure of the organism. Many of their effects may be called disease. Ancillary processes, thus, are a consequence of deleterious agents in the environment which are subject to some possible modification, whereas the determinate processes by their very nature are an inherent part of the machine.

It is, of course, apparent that ancillary processes may, in some respects, mimic the effects of determinate processes. Thus, while cell death may be a "normal" concomitant of aging on account of the way multicellular organisms are put together, or, for example, because of a continuation of some early process such as differentiation (for discussion see Ebert, 1959; Strehler, 1958), it is also apparent that external factors, such as irradiation, disease, physical damage, malnutrition, stress, etc., can produce cell death. *The central question we must ask regarding the possible acceleration of aging by ionizing radiation is not whether there is some similarity between the events which transpire in the absence of radiation and in its presence, but rather, the degree to which the two processes parallel each other in mechanism and in intimate effects on structures and functions. A simple life-shortening by radiation or any other deleterious agent is obviously not sufficient evidence that such an agent duplicates the effects of time.* On the other hand, the measurement of the effects of readily measured stresses, such as radiation, on the kinetics of death may furnish valuable clues for the formulation of a quantitative theory of mortality curves.

In the absence of detailed knowledge of the mechanisms underlying each of these processes, one cannot, at this time, reach firm conclusions about the extent to which radiation damage mimics or accelerates the normal aging process, or both. However, a useful comparison of these processes can be made even on the basis of the incomplete information available. The foundation of such comparisons consists of the general and specific matters set forth in the next three sections which deal with criteria of aging, a more detailed categorical analysis of possible aging processes, and a parallel examination of categories of possible radiation effects.

ON SOME CRITERIA OF BASIC AGE CHANGES

One of the primary goals of research in aging is the elucidation of the nature of the basic underlying changes in structure and function which lead to the gradual debility and eventual death of individual organisms. It is clear that a useful first step in such an undertaking is the

establishment of criteria (in essence, general though arbitrary definitions) of what constitutes or is meant by biological aging. These criteria would then act as tentative guideposts in the search for the underlying "key mechanisms."

We have elsewhere (Strehler, Mark, Mildvan, and Gee, 1959) set forth four such arbitrary criteria which we believe any age-associated change should meet before it is considered as a part of the basic aging process. These criteria are: (1) universality, (2) progressiveness, (3) intrinsicality, and (4) deleteriousness.

The basic postulate underlying these criteria is the following. There exist gradual changes in the structure of organisms which are not due to preventable diseases or other gross accidents and which eventually lead to the increased probability of death of the individual with advancing age. These changes represent the basic nature of the aging process (see also Medawar, 1951, and Comfort, 1956).

Although these changes may themselves produce a functional loss in the absence of environmentally induced age-correlated changes, they may also interact with the environmental influences to produce secondary change and disease.

The rationale behind the choice of these specific criteria is as follows:

1. *Universality. If the phenomenon is actually part of a general aging process, it should occur in all older members of a species, not just in certain of them.* This criterion eliminates many specific genetic aberrations and environmentally conditioned disease entities. Certain kinds of changes in older populations, which are not universal (for example, tumor occurrence), are not necessarily unrelated to basic age changes. For example, aging may be characterized by a decreased resistance to tumor development. The fact that some old individuals may not possess tumors is not evidence that an underlying change in resistance to tumors is not a universal concomitant of aging, for some individuals may not meet the challenge during their lifetime. Similarly, exceptional aged human beings possessing few or no arteriosclerotic lesions may demonstrate that arteriosclerosis is itself not a basic cause of aging, but, on the other hand, there may be common universal age-dependent changes in both affected and unaffected individuals which would produce vessel damage, if appropriate environmental factors, for example, nutrition, were altered.

In contrast to the above, any basic cause of age changes will be found to occur in all older individuals of a species.

2. *Intrinsicality.* This criterion, like that of universality, is designed to eliminate age-correlated changes which are not due to the design of the organism. Its inclusion, in addition to the criterion of universality, is necessitated by the fact that certain changes may be universal but still be the effects of the environment on the system. For example, some damage due to absorption of cosmic radiation will certainly occur in all long-lived animals, and such effects will therefore be universal. They are not, however, intrinsic to the system.

Intrinsic or determinate changes fall into three general categories:

A. Age changes genetically built into the system either by direct evolutionary selection or as disadvantageous byproducts of the evolutionary selection of an advantageous process.

Possible examples: Loss of ability to replace certain highly differentiated cell types after maturity.

B. Age changes which are genetically built into the system but which are not individually of sufficient consequence in terms of selection-pressure to have been eliminated.

Possible example: Pigment accumulation with advancing age in various fixed postmitotic cells.

C. Age changes which are due to internal disruptive events that occur without operation of specific genetic causes.

Examples: Denaturation, disorganization, entropy increase, and mutation.

In short, *intrinsic age changes are due to the design or operation hazards of any machine or to the inherent instability of any organized system in an energetic environment.* This subdivision of causes will be considered in greater detail in the next section.

3. *Progressiveness.* Since aging is considered a process rather than an event, it follows that its onset must be gradual and accumulative. Many age-correlated changes occur suddenly; for example; coronary artery occlusion (Lansing, 1952). They and their effects (scarring) are therefore eliminated as a basic part of the aging process, even were they to occur universally and intrinsically. *In general, processes may be viewed as*

the consequences of changes in small subunits of structures, for example, molecules or cells. It is this fact which gives them the outward appearance of progressiveness.

4. *Deleteriousness.* Finally, the age change should result in a decreased survival capacity of the old organism. Such a criterion is a direct consequence of the fact that the most characteristic property of aging populations is the increase in probability of death with advancing age. If there are universal, built-in progressive changes as animals age, these changes must also be capable of contributing to the increased death rate. Some age-correlated changes which meet the first three criteria may thus be eliminated as part of the basic aging process. They may, in short, simply be the final stages in adaptive processes and actually improve the organism's fitness. As such, they would be classified as part of development rather than aging. On the other hand, some developmental processes may become deadaptive in their terminal stages and thus meet all four criteria. Thus, although certain aspects of development may have great relevance to the basic biology of aging, it is equally apparent that this applies only to those developmental processes whose terminal stages are deadaptive or whose consequences involve a mixture of adaptive and deadaptive changes.

Although the above criteria appear reasonable from the biologists' standpoint, their application to specific phenomena is not a simple matter.

As regards universality, it is apparent that no series of measurements can embrace all individuals of a species. [While it may well be that there are many common mechanisms of aging among the various species and phyla, the discussion of universality is here limited to one species at a time.] Therefore, one can only estimate the probability that a phenomenon is universal on the basis of the size of the measured sample, the distribution of individual values, and the average change in the total population measured. Even in the absence of measurement, however, universality may be expected for certain changes on the basis of preexisting knowledge of a general nature.

Intrinsicality is perhaps the most difficult of the four criteria to evaluate unless the mechanism of the phenomenon is already understood. Lack of correlation with any modifiable environmental variable, except time, is perhaps the best test of this criterion.

Progressiveness of change can be established by measuring the same phenomenon repeatedly in the same animal throughout its lifetime. However, the usual cross-sectional age studies are not sufficient to meet this criterion unequivocally.

The deleteriousness of a given anatomical or physiological change depends in part on the environment in which the change occurs. Thus, a loss of visual acuity or of teeth is less of a problem to civilized man than the same defects would be to primitive individuals living on uncooked meat, inasmuch as means are available in civilized lands which effectively compensate for these defects. Similarly, changes which were highly detrimental or even fatal a few decades ago (for example, decreased resistance to infectious diseases among older animals) may no longer be so in civilized countries because of the advance of public health measures and the development of antibiotics.

Nevertheless, certain changes might be expected to be harmful in spite of environmental control or prosthetic measures. Correlation of the degree of age change with a decreased survival capacity is one means of establishing a presumptive relationship between the change and its possible effects. However, such correlations or the lack thereof may be misleading for the following reasons. Firstly, any age-correlated process will also, of necessity, be correlated with a higher mortality rate. Secondly, if the change (A) is correlated with some other process (B) which is the real deleterious agent, one might reach a false conclusion of causality between the deleterious effect and (A).

Conversely, the lack of demonstrable correlation between a change and the mortality rate does not rule out the change as a deleterious one, particularly if certain diseases or other major causes of death predominate.

In summary, it should be pointed out that much of the data, available in any such field as aging research, will permit only correlative conclusions rather than causal ones. It is hoped that the future will yield a greater volume of information which can be evaluated in causal terms especially as it applies to the underlying mechanisms.

EVOLUTION AND DETAILED CATEGORIZATION OF AGE CHANGES

In the preceding sections several categories of age changes were enumerated. These were particularly (a) the determinate processes of aging and (b) the ancillary processes due to preventable disease, accident, or other manipulable environmental factors. During the discussion of the determinate (or intrinsic) processes, three categories of such processes were enumerated. The ancillary processes constitute a fourth category of age changes. In this section we shall consider, in somewhat greater detail, the relationships between and the origins of these four categories of events.

Table 1 outlines some of these relationships. Note that the manifest change of general interest (the decreased survival capacity of the individual) is based upon a hierarchy of events proceeding from the elementary interactions of molecules at the cellular or subcellular level to the very complex interactions of a whole organism and its environment. Each higher level of function or organization is ultimately dependent upon some less complex phenomenon, structure, or process.

At the base of all these changes, however, lie the four sources of adverse change at the molecular or the cellular level (or both). It should be emphasized that it is at these levels that the ultimate decisions in evolutionary selection are made; that is, genes affect function and survival capacity solely by their effects on the kinds and rates of various molecular reactions they control, directly or indirectly, at the cellular level.

Organisms may be viewed as systems of collaborative catalysis which (teleologically speaking) make use of environmental matter and energy in their sole object of self-duplication.

In the long-term view, the probability of finding a representative of a given genetic line or species depends on the weighted sum of two processes that may be in some conflict, namely, (1) the rate or efficiency of reproduction, and (2) the survival capacity of the individual carrier of the germ line. The optimization of the first process, in a carefully controlled milieu, is achieved at the expense of the survival capacity of the individual organism in a less favorable environment.

Metazoan evolutionary progress has generally been in the direction of greater and greater ability to deal with the inhospitable environment (or, in some cases, to modify it). In many cases, this specialization is at the expense of reproductive rate—for the same space, energy, and matter cannot be used simultaneously for the germ line and soma.

But here a major biological paradox occurs, for whereas specialization and complexity have survival value for the species, the specialization of non-reproductive cells, as supporting and shielding structures for the germ line, is clearly at the base of the phenomenon of organismal senescence. It is the complexities of interdependence of the metazoan organisms and the loss of reproductive capacity of the soma that are the seeds of essential decay, senescence, and death.

Generally, one might expect that the soma-superstructure would evolve in such a manner that it potentiated reproduction. Changes beyond the normal reproductive period would not be subject to selection except, in special cases, where a strong interdependence existed between individuals of several generations. This secondary survival value of longevity might be expected particularly to be manifested in communicating social animals such as man, where the survival of the dependent young depends both on the persistent vigor of the parent and the accumulated experience of the "wise old man" of the social group. The female menopause may be an evolutionary device to insure the presence of the mother during the maturation period of the child.

However, even in non-social animals, we would expect some survival of the parental generation beyond the reproductive period, for as Comfort has so clearly pointed out, one of the factors which promote effective reproduction is general vigor (see Clarke and Maynard-Smith, 1955). It would be mechanistically unreasonable to expect vigor to cease or disappear at the instant of the cessation of reproduction, except in very special cases such as that of the salmon.

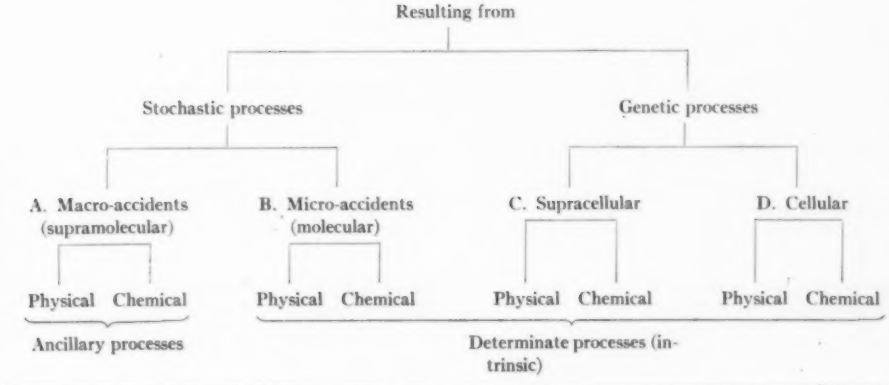
Nevertheless, even in the presence of these evolutionary factors which tend to select for longevity, all, or nearly all (see Bidder, 1925; Comfort, 1956) metazoans senesce; that is, they accumulate adverse change.

These adverse changes in aging may be looked upon as deficiencies in the design features of organisms. Design features are expressions of gene action and are themselves subject to genetic modification or to varying degrees and kinds of selection pressure.

TABLE 1

Origin and Relationships of the Categories of Age Changes

LEVEL OF ORGANIZATION	MANIFESTATION	MEASURE
Population	Increased probability of death (Aging)	Mortality rates
Individual	Decreased adaptation	General performance, Morbidity
Integrated function (Organ system)	Decreased ability to perform special functions	Physiologic tests
Tissue	Changes in tissues	Histological changes, Biochemical tests
Cell	Changes in cells	Histology, etc., Cell physiology
Subcellular elements and molecules	Changes in subcellular elements or extracellular environments such as a. nuclei b. membranes c. particulates and other organelles d. solutes e. stroma Arising from changes in a. synthetic rate b. utilization rate c. transport rate d. storage rate (e.g., formation of ppt., exhaustion of store)	Histochemistry, Biochemistry



Now, selection pressure will generally be directed toward the maintenance of the individual genetic carrier through the reproductive period and, as studies on the mortality of wild populations so clearly show (see Comfort, 1956), the most important factors limiting survival and causing mortality are the dangers and inhospitalities of the environment. *Natural selection will, therefore, result in the survival of design characteristics directed toward the attenuation or counteraction of these most prominent causes of death either by a shortening of the pre-reproductive period or by an increase in the vigor or ingenuity of the organism's capacity to adapt to, escape from, modify, control, or predict his environment.*

As a consequence of the predominance of the external environment in selection pressure, the other design features capable of leading to organismic decline and death (aging) will only become important when the environment is sufficiently hospitable that it is not the predominant cause of death. These factors are enumerated in Table 2. Note that Group 1 leads to the ancillary causes of aging discussed earlier, while Groups 2, 3, and 4 produce the intrinsic changes.

Of the four factors basically producing change at the molecular or cellular level, only one (macroscopic accidents) can be expected to be altered appreciably by modification of the environment. The other three basic groups of causes of senescence are probably only susceptible to evolutionary selection or to specific prosthesis in certain cases; for example, reading glasses or false teeth. *Stated otherwise, while we may expect eventually to control the environment and its challenges with great precision, it is not so likely that we will be able to compensate completely for errors, contradictions, or omissions in design,* that is, for changes in structure which are engendered by the rate of entropy increase in a non-reparable system. *These changes can best be attenuated by modifications in design, and such modifications are usually achieved by the interaction of genetic variation and selection pressure.*

Let us now consider, in somewhat greater detail, the nature of the stochastic and genetic causes of aging (structural alteration). Each of the major kinds of alterations of structure can be subdivided into two subcategories: physical causes; and chemical agents producing disruptive changes.

A. Macro-accidents or events (see Table 3-A), (that is, events involving simultaneous effects on

TABLE 2

Design Deficiencies

Changes in cells or their extracellular environment

Result from failure of design to take into account deleterious effects of

Accidents		Genetics and development	
1. Inadequacy of design	2. Omission of design	3. Errors in design	4. Contradictions in design
(Inability to repair and/or avoid gross damage)	(Inability to repair effects of micro-accidents)	(Presence of slow, but harmful side reactions a. catalysed b. uncatalysed)	(Opposing effects of same design feature a. at different time b. in different cells c. in different environments)

a large number of molecules or even the whole organism), have two features in common:

1. They are usually due to external (that is, environmental) causes.
2. They are, in principle, usually capable of prediction, and therefore are frequently subject to modification or control. Macro-accidents may alternatively be defined as local disruptive conditions (frequently due to energy concentration) which would not be expected on the basis of random events at the molecular level. They thus involve organized or unorganized aggregates of molecules, and it is their size which permits their general predictability.

In the case of man, his development of intelligence and his organization of societies and civilizations has operated to minimize these environmental inhomogeneities and inhospitalities through direct modification, group effort, measurement, recording, and prediction of natural forces and future events. A detailed listing of individual agents capable of producing gross disruptions directly is shown in Table 3-A.

B. Micro-accidents: This important source of the instability of any system involves the interaction of one or a few molecules. *Any structure will have an inherent instability if it is subject to local energy fluctuations which exceed the bond energies maintaining structure. Such local energy can, in principle, arise from only three types of events: heat, radiant energy, or chemical reactions* (see Table 3-B.).

1. Random local fluctuations in energy about

TABLE 3-A

Stochastic and Genetic Causes of Aging

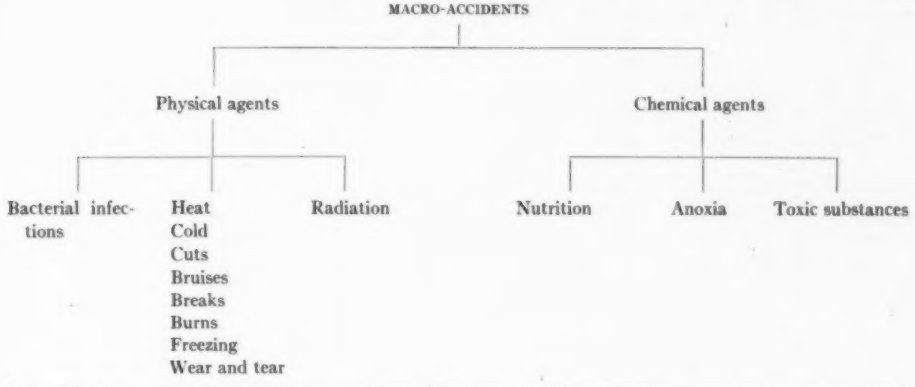


TABLE 3-B

Stochastic and Genetic Causes of Aging

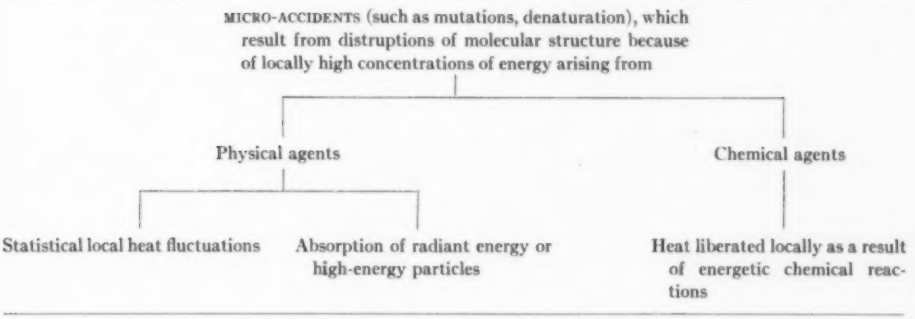
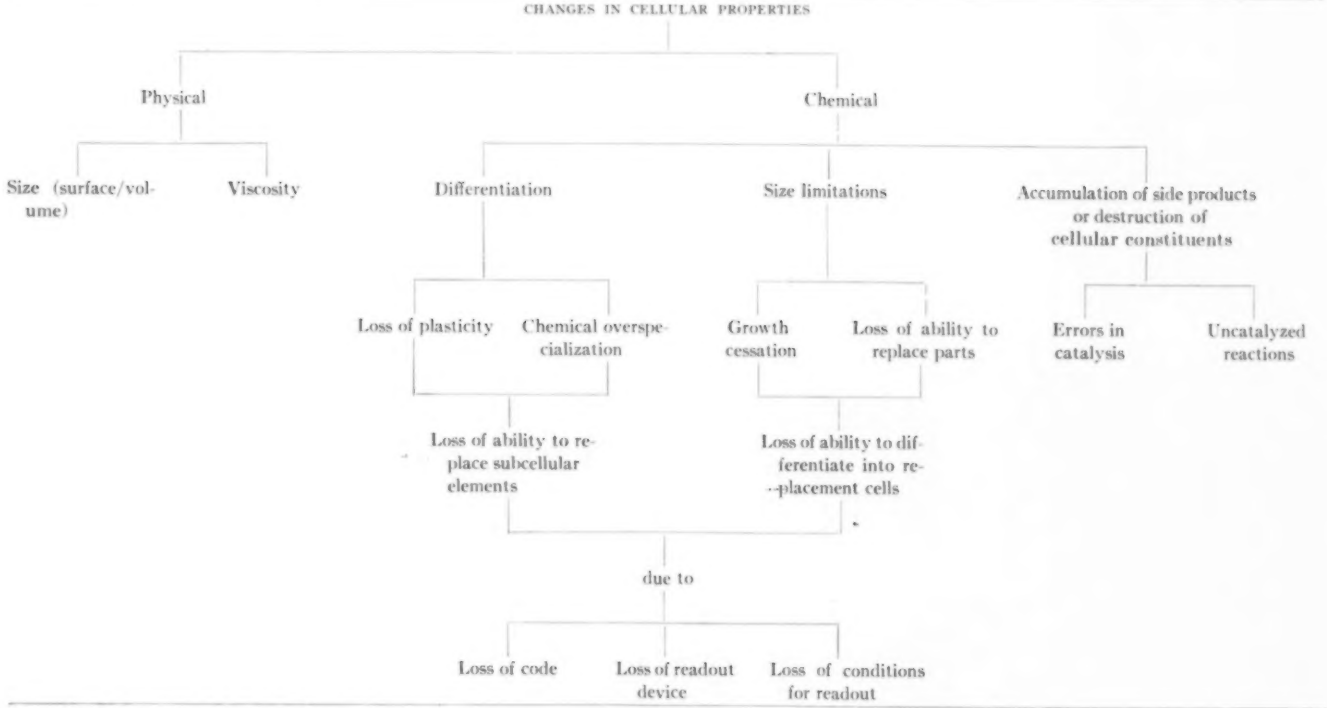

MICRO-ACCIDENTS (such as mutations, denaturation), which result from distruptions of molecular structure because of locally high concentrations of energy arising from
Physical agents
Chemical agents
Statistical local heat fluctuations
Absorption of radiant energy or high-energy particles
Heat liberated locally as a result of energetic chemical reactions

TABLE 3-C

Stochastic and Genetic Causes of Aging



some average value, as a result of the operation of the Maxwell-Boltzmann distribution law, will occasionally result in local energy concentrations sufficiently high to cause the alteration of structures in the vicinity.

2. A second means, by which molecules or polymolecular structures may become unstable, is through the localization of energy as a result of the absorption of radiant energy. For a short time after the absorption of a quantum of light, the absorbing system will be in an excited state. The energy stored temporarily in the excited electronic state will shortly be dissipated in one of four ways (see Franck and Platzman, 1954):
   a. Reemission of light (fluorescence or phosphorescence).
   b. Chemical reaction between the unstable or excited state and some molecule in the environment.
   c. Disruption of the excited molecule before its energy can be dissipated.
   d. Conversion of excitation energy in local heat energy.

Clearly, possibilities b, c, and d can lead to alterations of structures either of the absorber or of neighboring molecules.

3. The third source of molecular disruption is the liberation of locally high concentrations of energy as a result of the occurrence of a chemical reaction. The energy available per two electrons in a biological system is maximally about 40–60 kcal, while most reactions are considerably less energetic, for example, 5–15 kcal. The former energies are sufficient to disrupt many molecular structures, particularly those involving hydrogen bonds, whereas the latter can operate primarily to facilitate reactions by adding their energy to the Maxwell-Boltzmann fluctuations.

It should be emphasized that the energy available locally may be considerably greater than the free energy liberated by the reaction. This surprising fact is a consequence of the fact that a molecule must absorb thermal energy before it can react. When the products are formed, however, this energy plus the free energy of reaction are liberated locally. Stated otherwise, the energy available locally at the termination of a chemical reaction is equal to the activation energy of the reverse process. Since catalyzed reactions are characterized by lowered activation energies, it likewise follows that the local energy possessed by the products will be less for catalysed reactions than for uncatalysed ones. *Enzymes thus function to decrease the probability of damage per reaction as well as to speed up the rate of reaction.*

C. Cellular changes (see Table 3-C): *In the most general sense, the chemical constitution of cells will change when the rate at which each substance appears* (either by synthesis or transport) *is not equal to the rate of its disappearance* (either by transport or utilization). The chemical differentiation processes in development represent a controlled change in constitution directed toward the production of functionally specialized cells or multicellular structures. By contrast, *aging may be viewed as change in constitution due to the inequality of the rates of appearance and disappearance of specific chemical structures, changes which are not directed toward the production of a more effectively adapted organism.*

The sources of these alterations may be accidental or genetic, polymolecular or unimolecular, unicellular or organismic, intracellular or extracellular.

At the cellular level, those changes which are genetic in origin are detailed in Table 3-C. These changes are produced, in turn, by changes in one or more of the following factors in such a manner that the steady state is incompatible with continued function:

1. Rate of synthesis
2. Rate of utilization
3. Rate of transport
4. Rate of storage or attrition of stores
5. Rate of entropy change (organization)

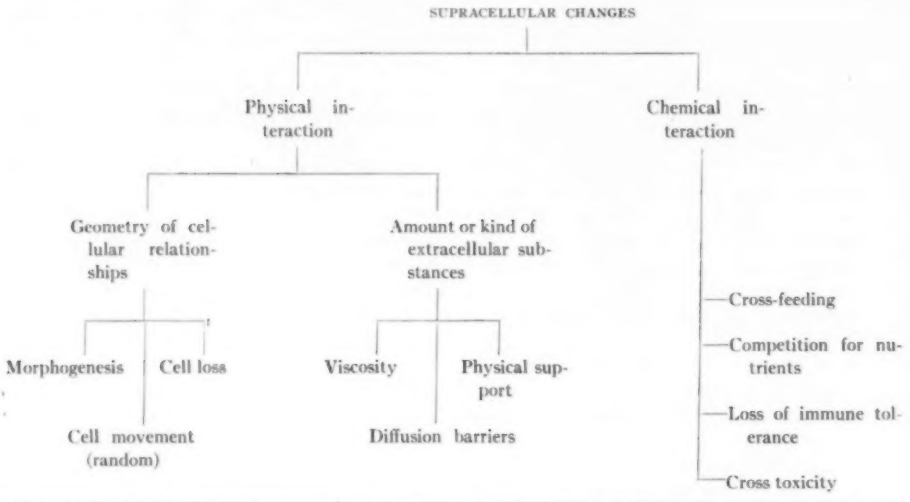
The various possible and published theories of the mechanisms of aging are simply expressions of the above hypothesis in various degrees of specificity, refinement, and sophistication.

The physical changes in cells which might lead to altered constitution are changes in size or arrangement and changes in viscosity, both of which produce effects on rate of transport.

The chemical changes include byproducts of catalysed or uncatalysed reactions (Sinex 1959), as well as differentiation and its sequelae, for example, loss of plasticity or possibly over-differentiation (see Strehler, 1958). The loss of

TABLE 3-D

Stochastic and Genetic Causes of Aging



plasticity hypothesis was particularly favored by Raymond Pearl (see Pearl, 1928).

Size limitation and its consequences for repair and chemical constancy have been discussed in detail by Comfort (1956) and by Bidder (1932). The mechanism of size control and differentiation will determine to a considerable extent the degree to which one might expect to effect modification of these gene-controlled processes by external chemical or physical manipulation. A loss of (1) code or information or (2) machinery for following the synthetic directions in the code would be considerably more difficult to repair or alter than (3) the conditions for readout. By analogy, the failure of a phonograph to make music might be due to (1) a loss of the record, (2) a defect in the player, or (3) simply due to the fact that someone disconnected the electrical supply.

The third category of chemical changes in cellular properties due to genetic factors is the occurrence of slow rates of chemical reactions between components. Such reactions may either destroy or alter structure or produce insoluble or toxic products which cannot be removed. These reactions might be due to errors in catalysis, that is, to non-specificity of the catalyst, or to non-catalyzed reactions between reactive intermediates in metabolism.

D. Supracellular changes (see Table 3-D): The kinds of age changes described in the preceding section may be expected in any organism, either single-celled or multicellular. However, multicellular organisms, despite the advantages inherent in their multicellular, specialized organization, face certain disadvantages as a result of their multicellular character. *These additional sensitivities arise from the fact that the same collaborative organization which permits the multicellular animal to survive more effectively in the face of a hostile environment, also demands a series of limitations on the capacities of the individual cells and, moreover, imposes a series of obligatory interdependences and interactions which introduce new sources and orders of instability.*

These instabilities result from either chemical or physical relationships or interactions between cells.

Physical and chemical interactions between cells are affected by:

(1) the geometrical relationship of one cell to another; and

(2) the nature of the non-living matter between cells.

The geometrical factor will be altered by changes in cell size, cell death, random cell migration, and by a continuation of morphogenetic

processes, for example, death of certain cells during morphogenesis (Glücksmann, 1951). By virtue of its effect on viscosity or because of the presence of physical barriers to diffusion, such as membranes, fibers, or particles, the nature of the intercellular substances will influence the physical support of cells, their mechanical coordination, and the access and egress of diffusible substances.

The chemical interactions between the cells of the multicellular organism obviously depend upon the kind and concentration of diffusible substances passing from one cell to another. These interactions involve inhibition or stimulation of cellular function by cross-feeding, competition for nutrients, reaction to toxic or regulatory substances, and possibly immunological tolerance manifestations.

Obviously, much of the above has been suggested or written earlier and eloquently by others (see Weismann, 1882; Pearl, 1928; Comfort, 1956; Medawar, 1951; Williams, 1957; Cowdry, 1952; Lansing, 1952; Shock, 1957; Clark and Pirie, 1957). Some of the possibilities here discussed may possess some novelty. *Nevertheless, we cannot yet decide which of these many alternatives are the major ones and, moreover, it is clear that all possibilities take place at some rate. The assessment of their relative contributions and the detailed underlying mechanisms are the major general scientific objectives of aging research.* It is hoped that this detailed dissection and categorization of the major and general possibilities will help others as it has aided us in our attempts to test and evaluate the relative contribution of various factors contributing to biological senescence.

SOME CATEGORIES OF POSSIBLE RADIATION EFFECTS WHICH MIGHT RESEMBLE AGING

In the foregoing section, we have considered the detailed sources of age change in biological systems. In order to evaluate the degree to which various radiation effects may accelerate the aging process by contributing to these changes, it might be instructive to examine briefly the kinds of effects which radiation is known to produce (see Hollaender, 1954).

The absorption of high-energy radiation by living matter results primarily in a disruption of chemical bonds in the absorbing structure (Franck and Platzman, 1954). If the disrupted structure is a functional one, the radiation may produce damage directly, but, since water is the most prevalent of absorbing materials, the products of its splitting, such as H and OH radicals, as well as other reactive products (O_2H, H_2O_2) (see Hollaender, 1954) derived from them, produce alterations of sensitive structures via secondary chemical reactions.

Effects on dividing cell lines

These physical and chemical effects of radiation thus produce changes which, in turn, affect any aspect of a cell's function. But, as might be expected, *the effect is most profound when the disruptive action affects those structures, of which only one or a few copies are present per cell, so that a loss of such a structure results in the loss or alteration of all functions of that cell dependent on the structure. Structures of this nature are genes, chromosomes, and associated organelles.*

Thus, if the disruptive action of radiation affects a genetic structure, that is, a gene, a chromosome, or an organelle concerned with mitosis (for example, certain nucleoli), it may result in a cell which is either incapable of dividing (Gaulden and Perry, 1958) or of producing a specific functional component whose synthesis depends on the gene (Muller, 1928; Beadle and Tatum, 1945).

Of course, radiation may also produce damage in non-genetic structures, but measurable immediate effects on function and metabolism (Sheppard and Stewart, 1952; Billen, Strehler, Stapleton, and Brigham, 1953) make themselves felt at dosages of radiation which are many times greater than those required for the production of a single mutation per cell or of a suppression of cell division (Hollaender and Claus, 1936; Atwood, 1954; Puck, 1957) by damage to the mitotic apparatus.

From the above considerations, it follows that the primary effect of radiation will be on cells which actively grow and divide in making their contribution to the over-all physiological economy of an organism. It is, therefore, not surprising that the short-term killing effects of radiation (Sacher, 1955; Boche and Bishop, 1951; Hursh and Casarett, 1959) appear to be due to a suppression of regular division and replacement cycles; particularly, as manifested by the blood-forming elements, gastrointestinal tract, and skin (Furth, Andrews, Storey, and Fish, 1951;

Bloom and Bloom, 1954; Jacobson, 1954). It is interesting also, in this regard, that organisms such as adult *Drosophila melanogaster* which have no regular cell replacement cycle, are remarkably durable to radiation and can resist dosages even as high as 100,000 r without appreciable life-shortening (Sacher, 1959). At dosages of 4,000–5,000 r, we have actually observed an increase (doubling) in the longevity of *Drosophila melanogaster* (Strehler, unpub.).

Even much of the delayed effect of radiation on the survival of multicellular organisms may be due to the effects on dividing cell lines. For example, the increase in cancer death rate following radiation (Furth and Lorenz, 1954) is an effect on a dividing cell line.

Life-shortening in irradiated animals, as a consequence of genetic or mitotic effects on dividing cell lines, can be due, in turn, to one of several mechanisms:

Firstly, the temporary depletion of the specific dividing cell line might produce a generalized damage to the organism, particularly to fixed postmitotic cells, and such damage might not be reparable after the stem cells have been restored.

Secondly, it might be that a selection process, following the radiation damage to the dividing cell lines, results in cells which are, for one reason or another, inferior in their capacity to carry out their normal function. Such an increasing incapacity would hasten aging and death, because of a decrease in the effectiveness with which fixed postmitotic cells carry on their functions.

To illustrate this point, assume that a cell line (for example, one of lymphocytes) contributes its role to the over-all bodily economy through the production of a specific product, protein *a*. Now, it is quite conceivable that various aberrant cell lines could be produced spontaneously or by radiation which might even fail to produce the specialized product. If we assume that the growth rate of a specific cell line is limited by (among other things) the rate at which it acquires building blocks for the specialized component, then it follows that a decrease in rate of synthesis of this specialized component will give a selective growth advantage to the "inferior cell." Thus, a genetic change which results in a cell with an increased survival capacity in its particular environment (the metazoan body) also results in a gradual deterioration of that environment.

Effects on non-dividing cell lines

The view has been expressed repeatedly that the primary effects of aging are on those differentiated, non-dividing cell lines known as "fixed postmitotics" (Cowdry, 1952). It has been shown, for example, that there is a gradual decrease in the number of cells in certain non-dividing cell populations with increasing age (Andrew, 1938; Corbin and Gardner, 1937; Gardner, 1940; Ellis, 1920). If radiation produces a loss of tissue cells, directly or indirectly, it may closely mimic these effects of time.

However, there are age changes which do not involve cell loss (Andrew, 1952; Jayne, 1950; Hyden and Lindstrom, 1950; Hamperl, 1934; Bommer, 1929; Stübel, 1911). For example, *much of the progressive change in histological structures, which has been described in association with the aging process* (Lansing, 1952), *takes place in or around the non-dividing fixed postmitotic cells and does not necessarily result in cell death.* We should, therefore, consider what kinds of effects radiation might have on these cell lines other than to kill them. These effects can be divided into four categories:

1. Effects on the nuclear genetic makeup of such cells. We cannot estimate the magnitude of radiation effects on the genetic makeup of non-dividing cell lines for, even if mutations were to occur (as they probably do), it is not known to what extent the differentiated cell is independent of its genome.

2. Effects on cytoplasmic replicating particles. Similarly, we cannot, at present, estimate the effects of time and radiation on cytoplasmic replicating particles. It is possible that studies of the sensitivity of differentiation in non-dividing cells toward radiation or, alternatively, of radiation effects on axonal regeneration, could furnish evidence permitting a tentative evaluation.

Such non-genic effects of ionizing radiation on the cytoplasm of cells might result in a long-term deleterious effect on the life or function of the affected cells. For example, radiation might induce the production of altered cytoplasmic templates for specific enzymes. The altered products of such cytoplasmic genes might, in turn, produce more and more of such aberrant tem-

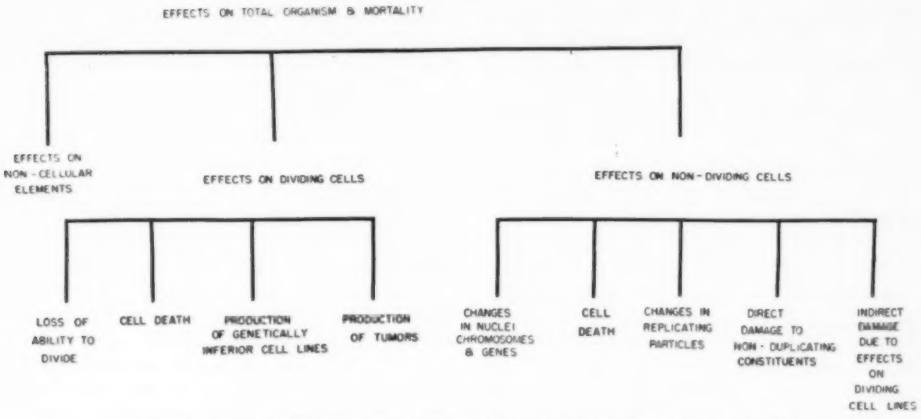

EFFECTS ON TOTAL ORGANISM & MORTALITY
EFFECTS ON NON-CELLULAR ELEMENTS
EFFECTS ON DIVIDING CELLS
EFFECTS ON NON-DIVIDING CELLS
LOSS OF ABILITY TO DIVIDE
CELL DEATH
PRODUCTION OF GENETICALLY INFERIOR CELL LINES
PRODUCTION OF TUMORS
CHANGES IN NUCLEI CHROMOSOMES & GENES
CELL DEATH
CHANGES IN REPLICATING PARTICLES
DIRECT DAMAGE TO NON-DUPLICATING CONSTITUENTS
INDIRECT DAMAGE DUE TO EFFECTS ON DIVIDING CELL LINES

FIG. 4. SUMMARY OF MANNER AND LOCUS OF POSSIBLE RADIATION MIMICRY OF AGING

plates and products, and thus the cell might gradually change or die after the passage of considerable periods of time without manifesting any immediate effects.

3. Effects on irreplacable structures and molecules. Into this category fall such events as the destruction or alteration of extracellular structures (for example, connective tissue elements), enzymes, microsomes, mitochondria, membranes, and various organelles concerned with the continuing function of cells. If we assume that the long-term effects of radiation on such structures are similar to their short-term effects, it would appear that the dosage required to produce nongenic radiation effects is far in excess of that required to produce the well-known shortening of the life span. Relevant to this judgment is the fact that very large dosages are required to kill organisms, such as *Drosophila,* which contain no dividing cells other than those connected with reproduction.

4. Effects indirectly due to changes in dividing cells lines upon which the non-dividing lines depend. Casarett (1959) has recently reported that the course of events intervening between radiation and tissue atrophy suggests that much of the cell death and hypoplasia may be secondary to effects on the vascular cellular elements (which cells appear to be more sensitive).

To recapitulate, the potential sites of action of ionizing radiation in producing a decreased functional capacity of an organism are two in number: first, the fixed postmitotic cells, which have differentiated, can no longer divide, and cannot be replaced; and second, the actively mitotic cells, characteristic of those tissues and organs which replace themselves on a regular schedule (blood, skin, intestinal epithelium) or on demand (liver, tubular epithelial cells of the kidney) (see Fig. 4).

Superficially, at least, there seems to be a contradiction between the effects of radiation and of time. On the one hand, the most profound changes during the aging process involve fixed postmitotic cells, and on the other hand the short-termed lethal effects of radiation generally appear to be due to the depression of mitosis in the stem-cell lines of the normally replenishing tissues (Patt and Brues, 1954). If radiation produces an acceleration of the aging process, we should expect the long-term effects to be mainly in the fixed postmitotics. Alternatively, there might be damage to mitotic cells which are not made manifest until long after the animal has "recovered." These alternatives cannot be readily tested because one cannot irradiate the mitotically active cells without also irradiating certain of the non-mitotic cells of the body. However, an index of the degree to which the long-term life-shortening effects of radiation are due to effects on mitotically active cells might be ascertained by studying the longevity and actuarial behavior of animals which have received higher doses of radiation in tissue sites which are not primarily mitotic (central nervous system, heart, musculature, etc.). The dosages

required to kill animals thus exposed are considerably higher than those required to kill with whole-body radiation (Jacobson, 1954).

ANALYSIS AND DISCUSSION OF SPECIFIC THEORIES OF RADIATION EFFECTS AND AGING

We now proceed to analyze some of the specific theories of aging which have been suggested to explain life-shortening effects of radiation.

Connective tissue changes

It is known that there are considerable changes in the properties of the connective tissue of the body of human beings and of experimental animals during the normal aging process. These changes result in gross alterations in the texture and elasticity of the skin and other organs, and have been subjected to quantitative measurement both in the hands of biochemists and of physiologists. Of particular note in this regard are the researches of Gersh and Catchpole (1949), Verzár (1957), Sobel and Marmorston (1956), Gross (1958), and their collaborators. Verzár (1955) has developed a test of an animal's (rat's) physiological age on the basis of the rate of shrinkage of its collagenous tail tendon fibers when they are exposed to high temperatures (ca. 60°C) in vitro. In order to test the possibility that ionizing radiation directly affects the properties of the connective tissue, Verzár (1959) in Switzerland, and Sinex (1959) in this country, have subjected rat tails to large doses of ionizing radiation. The irradiated rat tail collagen was not altered by comparison with unirradiated control collagen. If rat tail tendon collagen, which normally undergoes a striking agewise change, can be considered as representative of connective tissue generally, then it appears that, at least in so far as the changes in collagen which parallel aging are concerned, there is a dissimilarity between the effects of time and those of high-energy radiation.

Vascular inadequacy

Another specific theory of aging, which has received some favor over the years, considers the decline in function which takes place with advancing age to be due to a loss of parenchymal cells in the various organs, or to a decreased efficiency of their function. This decreased function may, in turn, be due to a gradual failure of the circulatory system, particularly of the capillary network (Landowne, Brandfonbrenner, and Shock, 1955; Landowne, 1958). It is well known that there is a continual increase in the amount of pathological conditions as a human population ages and that one of the major sites of such pathological condition is the circulatory system. In the present context, if radiation were to produce a gradual or a sudden disruption of the effective functioning of the circulatory system, various unhappy results might be expected to follow, including a shortening of the life span. To the extent that any changes induced by radiation parallel in detail the tissue pathology of normal senescence, the former may be regarded as an agent promoting premature senescence. On the basis of his studies on a large sample of irradiated mice and rats, Casarett (1959) has proposed that radiation does indeed produce parenchymal cell and tissue atrophy, but he also has suggested that such changes, when induced by radiation, are somewhat different in their temporal sequence from the normal course of events with the passage of time. On the other hand, it cannot be considered to be established that the decreased functional capacity which gradually takes place in human beings as they grow older is, in all old persons, associated with or due to a decreasing number of viable tissue cells. Qualitative cell changes may be equally important.

Somatic mutations

It has been suggested by Henshaw (1947) and Failla (1958, 1959a) that the normal aging process is characterized by, and perhaps is due to, an accumulation of somatic mutations. Since the main recognized effect of ionizing radiation on the germ line is the production of gene and chromosomal mutations, the Failla theory is particularly attractive in that it suggests a definite mechanism whereby ionizing radiation could produce defects in function reminiscent of the effects of time. Therefore, the pros and cons of this general theory will be considered in some detail. Since the Failla theory deals largely with mutations in differentiated cells which have already ceased to divide, it could be labeled the theory of aging by mutation of fixed postmitotic cells.

Pro: Among the most interesting of the arguments indicating that time and radiation have similar effects is the fact that radiation may be

substituted for time in producing certain modifications of mortality rates.

A second argument consistent with the theory is the fact that, with the exception of cancer which seems to be uniformly increased in its incidence in radiated animals, the incidence of specific diseases does not appear to be remarkably altered (Furth et al., 1954). Such diseases as amyloidosis merely occur earlier in the life cycle and run out their courses earlier (Sacher, 1959). A third argument given in support of the theory is the fact that many of the deaths induced by radiation cannot be attributed to any specific cause, but to a rather diffuse deterioration (Furth et al., 1954) analogous to that which has been observed in the "normal aging process." Finally, it has been pointed out that the life span of various species is roughly inversely proportional to the germ line mutation rate of that species (Failla, 1959a). This is certainly the relationship to be expected according to the above theory (Casarett, 1959).

Con: Despite the attractiveness of the theory, and the existence of a body of evidence which suggests that there is some relationship between radiation damage and the normal aging process, there is some rather convincing evidence which points in the opposite direction, namely, that radiation shortens the life span by other means than purely through an acceleration of the normal effects of time. The first of these arguments is a general one: that is, it is highly unlikely that two such different physical agents as time and radiation should produce exactly parallel or identical changes in such multicellular organisms as the human being or rat, which are subjected to so many different kinds of dysfunction, disease, and pathology. Thus, although there may be a unitary mechanism underlying most of the aging process, this process manifests itself in quite different ways in different individuals and different species of animal. Since there are many conceivable ways in which a complicated interdependent chemical system such as a living being might deteriorate with time, it would be surprising if, in all respects, the effects of time paralleled the effects of high-energy radiation.

Also, at the molecular level, it would be surprising if the two events were the same, since ionizing radiation possesses energy in terms of kilovolts, whereas the disruptive effects of thermal accidents, or of "accidental" chemical reactions yield local energies of only a few volts at most. It appears unreasonable to expect that thermal denaturation of sensitive structures or the combination of one or another sensitive molecule in a cell with an accidentally produced free radical, on the one hand, would imitate closely the gross molecular disorganization which radiation produces.

Secondly, although Failla's theory assumes that the increased mortality rate is the reflection of an inversely decreased "vitality," it should be pointed out that we cannot assess the quantitative effect on function of a given frequency of mutation in the somatic cell lines, or its effect on life-shortening. Thirdly, it is not at all certain that the sensitivity of the somatic line is similar to that of the germ line, either as regards the frequency of occurrence of mutation or the extent and severity of consequent deleterious effects in the adult organism. It could well be argued that the cells of multicellular organisms make use of nutritional interdependence or cross-feeding mechanisms which are not available to the germ line.

Fourthly, in addition to these general arguments against mutation as the primary mechanism of aging (upon which, it can be argued, hangs the general validity of the assumption that radiation and time produce similar events), there are a number of specific experimental findings which are in conflict with the theory.

If we assume that there is some similarity between the aging of an invertebrate such as *Drosophila* and that of human beings, then we would expect that ionizing radiation should also produce a life-shortening of this animal so greatly used as an object of research on aging. Ionizing radiation, even in enormous dosages of 50,000 or 100,000 r, does not appreciably shorten the life span of *Drosophila* or other insects (Sacher, pers. commun.; Strehler, unpub.). Moreover, even among mammals, it has been shown that moderate dosages of radiation will actually, in some instances, increase the life span. For example, female mice live considerably longer than normal, if they are subjected to as much as 100 r early in life. This phenomenon, noted by Sacher (1956) and by Gowen (1959) independently, has been ascribed by the former to a specific heightening of the resistance to certain kinds of diseases and by the latter to the fact that irradiated female mice are sterile and, there-

fore, undergo less of the risks associated with litter bearing.

Fifthly, while it has been said by some pathologists that there are no striking differences between the patterns of pathology in irradiated or unirradiated mice allowed to age normally, it is quite evident that certain kinds of diseases are produced in much greater abundance in irradiated mice. These diseases are particularly various kinds of cancer. If radiation were to mimic the effects of time exactly, the disease pattern should not be altered. A Gompertzian analysis of irradiated and unirradiated animals, excluding deaths due to tumors, would be of interest. It is also quite important to point out that the pattern of specific disease pathology may have little bearing on the similarity or dissimilarity of the underlying processes causing an accelerated appearance of diseases. Thus, it would be surprising indeed if treatment by high-energy radiation which resulted in a high percentage of cell loss and abnormality, perhaps regardless of the cell type involved, did not also produce an accelerated incidence of such diseases as normally befall the organism when his cellular reserves fall below a certain level. But this general similarity says little about underlying similarities in mechanism.

Sixthly, many of the most profound effects of time are on the fixed postmitotic cells of the body. On the other hand, radiation kills selectively the dividing cell lines. Such disparity in locus of action should certainly produce different detailed pictures of change.

The final argument against the assumption that radiation produces an acceleration of the normal process of aging is based on the quantitative contrast between the effects of dose on life-shortening on the one hand, and of dose on mutation rate in the germ line, on the other hand. If we assume that the germ line and somatic cells are approximately equally sensitive to radiation (in terms of yield of mutations per roentgen), then, as Failla (1959b) has pointed out, it should be possible to calculate the radiation dose to which the normal rate of aging is equal. This can be done by measuring the amount of radiation which is required to double the rate of aging as measured by the Gompertz slope. Failla (1958) has calculated this relationship, and it turns out to be approximately 12 r per day as a doubling dose for a certain strain of mice. It is known from other genetic experiments that the doubling dose for mutation of the germ line is about 0.5 r per day. Thus, there is a difference of about a factor of 25, either between the effectiveness of radiation in producing somatic mutations, or in the ease with which they express themselves in somatic cells by life shortening.

Note particularly that in Fig. 3 the best straight line does not pass through the origin. Therefore, it appears that the increase in Gompertz slope due to low doses of radiation is considerably greater than the increase in slope produced by the same dose when it is added to a larger background dose; that is, there is a decrease in the effectiveness of radiation in increasing the Gompertz slope. This suggests that two types of damage or two subpopulations are involved. Possibly the initial effect is due to one type of damage (for example, production of tumors), while the latter effect reflects more general or widespread damage.

Thus the theory makes assumptions which are in quantitative conflict with observation. In fairness to the theory, it should be pointed out that it is quite possible for somatic mutations to contribute substantially to the normal aging process and also that radiation effects may accelerate some important reaction contributing to the over-all aging process. The above arguments thus do not rule out somatic mutation as a part of the aging process. Indeed, it would be difficult to imagine an organism in which the occurrence of somatic mutations would be completely absent.

But the above considerations do cast doubt upon the quantitative importance of such a somatic mutation process in aging and, at the same time, places under the shadow of doubt the general theory of the identity of time and radiation effects on the functional capacities of organisms.

In the opinion of the writer, if mutations are to contribute effectively to the aging process, they might be expected to do so quite differently in the fixed postmitotic cells and in those cells which are continually in a process of replacement. In these latter cell lines, a selection such as was described in the earlier section could contribute to normal aging and could likewise be accelerated by radiation. The arguments relating to dose and life-shortening need not apply to this kind of a cell line, since the effectiveness of such events in shortening the life span depend (1) upon how frequently they occur, (2) on how much time is required to make the effects felt, and (3) on the magnitude of the ultimate effects.

CONCLUSIONS

It has been shown that the process of aging can be viewed as the sum total of those changes in structure (and consequently in function) which take place following reproductive maturity, changes which result in a decreased adaptation to the environment and which are reflected in a decreased survival capacity, that is, an increased mortality rate. The inadequacy of most mathematical-physical theories of mortality rates is demonstrated.

Since all changes affecting the fitness of organisms are basically changes in the kind, amount, or arrangement of molecules and cells, the sources of such changes have been enumerated and analyzed. The changes were shown to arise from two basic kinds of causes: stochastic processes and genetic processes. Aging was defined as those changes which are due to genetic factors and to disruptive accidents on the molecular level. A series of four criteria that basic biological age changes should meet were tentatively set forth. These are: (1) universality, (2) intrinsicality, (3) progressiveness, and (4) deleteriousness.

A dissection of the evolutionary origin and nature of the possible sources of instability (change or aging) of biological systems and of evidence bearing on them makes it eminently clear that:

(1) a multiplicity of causes of aging are operative; and

(2) it is not at present possible to assign relative weights to the various possible processes. This is the general goal of aging research.

With this multiplicity and consequent uncertainty in mind, the thesis that radiation-induced life shortening of experimental animals is an acceleration of the "normal aging process" has been examined critically.

On the basis of a detailed analysis of the possible sites of major radiation effects, the following conclusions appear justified:

1. The primary sensitive site of radiation damage is the genetic apparatus of dividing cells, whereas the principal changes associated with aging appear to take place in non-dividing (fixed postmitotic) cells.

2. Certain organisms which show marked age changes are remarkably insensitive to radiation. It, therefore, appears unlikely that they age by somatic mutation processes.

3. Radiation exposure does not produce in certain connective tissue elements (collagen) changes that are analogous to normal age changes.

4. The radiation dose required to double the rate of "aging" of rats (as measured by the rate of increase of mortality rate) should produce about twenty-five times the basal number of mutations (assuming equal effectiveness of radiation on the germ line and soma) rather than a simple doubling; that is, the life-shortening and mutational efficiencies are apparently quite different.

Generally, although certain tissue changes in response to radiation (particularly cell loss) are reminiscent of parts of the normal aging process, it appears unlikely on the basis of the above facts that there is a detailed identity between the effects of time and radiation. Aging is probably a more complex phenomenon in its origins and mechanisms than radiation life-shortening. Unless one is prepared to entertain a series of special ad hoc assumptions, the evidence already available makes it appear unlikely that somatic mutation is a quantitatively important part or cause of normal aging.

LIST OF LITERATURE

ANDREW, W. 1938. The Purkinje cell in man from birth to senility. *Z. Zellforsch.*, 28: 294.

——. 1952. *Cellular Changes with Age.* 74 pp. Charles C Thomas, Springfield, Ill.

ATWOOD, K. C. 1954. Ultraviolet effects on Neurospora heterokaryons. *Proc. 1. Intern. Photobiol. Congr.* (4. Intern. Light Congr.), 143–145.

BEADLE, G. W., and E. L. TATUM. 1945. Neurospora II. Methods of producing and detecting mutations concerned with nutritional requirements. *Amer. J. Bot.*, 32: 678–686.

BERLIN, N. I., and F. L. DIMAGHO. 1956. *A survey of theories and experiments on the shortening of life span by ionizing radiation.* Armed Forces Special Weapons Project, Technical Staff Study No. 608, Washington, D. C.

BIDDER, A. P. 1932. Senescence. *Brit. med. J.*, 2: 5831.

BILLEN, D., B. L. STREHLER, G. STAPLETON, and E. BRIGHAM. 1953. Post irradiation release of adenosine triphosphate from *E. coli* B/r. *Arch. Biochem. Biophys.*, 43: 1–10.

BLOOM, W., and M. A. BLOOM. 1954. Histological changes after irradiation. In *Radiation Biology*, (A. Hollaender, ed.), I, Part 2, 1091–1143. McGraw-Hill Book Co., New York.

BOCHE, R. D., and F. W. BISHOP. 1954. Studies on the effects of massive doses of X-radiation on mortality in laboratory animals. In *Biological Effects of External Radiation*, (H. A. Blair, ed.), pp. 3–10. McGraw-Hill Book Co., New York.

BOMMER, S. 1929. Weitere Untersuchungen über sichtbare Fluoreszenz beim Menschen. *Acta derm.-venereol., Stockh.*, 10: 391–445.

BRODY, S. 1923. The kinetics of senescence. *J. gen. Physiol.*, 6: 245–257.

BRUES, A., and G. SACHER. 1952. Analysis of mammalian radiation injury and lethality. In *Symposium on Radiobiology*, (J. J. Nickson, ed.), pp. 441–465. John Wiley & Sons, New York.

CASARETT, G. W. 1959 (in press). Acceleration of aging by ionizing radiation. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

CLARK, F. L., and N. W. PIRIE. 1957. Introduction. In *Biology of Aging*, (W. B. Yapp and G. H. Bourne, eds.), pp. ix–xiv. Hafner Publishing Co., New York.

CLARKE, J. M., and J. MAYNARD-SMITH. 1955. The genetics and cytology of *Drosophila subobscura*. XI. Hybrid vigor and longevity. *J. Genet.*, 53: 172–180.

COMFORT, A. 1956. *The Biology of Senescence*. 257 pp. Rinehart & Co., New York.

CORBIN, K. B., and E. D. GARDNER. 1937. Decrease in number of myelinated fibers in human spinal roots with age. *Anat. Rec.*, 68: 63–74.

COWDRY, E. V. 1952. Ageing of individual cells. Chap. 3 in *Cowdry's Problems of Ageing*, (A. I. Lansing, ed.), 3rd Edition, pp. 50–88. Williams & Wilkins, Baltimore.

CURTIS, H. J., and R. HEALY. 1958. Effects of radiation on aging. *Advances in Radiobiology*, pp. 261–265. Oliver & Boyd, Ltd., Edinburgh.

DAVIES, D. F., and N. W. SHOCK. 1950. Age changes in glomerular filtration rate, effective renal plasma flow and tubular excretory capacities in adult males. *J. clin. Invest.*, 29: 496–507.

EBERT, J. 1959 (in press). Comments. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

EDEN, M. 1959 (in press). An analogy between probabilistic automata and living organisms. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

ELLIS, R. S. 1920. Norms for some structural changes in the human cerebellum from birth to old age. *J. comp. Neurol.*, 32: 1–33.

FAILLA, G. 1957a (in press). The aging process and somatic mutations. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

——. 1957b (in press). Comments. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

——. 1958. The aging process and cancerogenesis. *Proc. N. Y. Acad. Sci.*, 71: 1124–1140.

FALZONE, J. A., and N. W. SHOCK. 1956. Physiological limitations and age. *Publ. Hlth. Rep., Wash.*, 71: 1185–1193.

FRANCK, J., and R. PLATZMAN. 1954. Physical principles underlying photochemical, radiation-chemical and radiobiological reactions. In *Radiation Biology*, (A. Hollaender, ed.), Vol. I, Part 1, pp. 191–253. McGraw-Hill Book Co., New York.

FURTH, J., G. A. ANDREWS, R. H. STOREY, and L. WISH. 1951. The effect of X-irradiation on erythrogenesis, plasma and cell volumes. *Soc. Med. J.*, 44: 85–92.

——, and E. LORENZ. 1954. Carcinogenesis by ionizing radiation. In *Radiation Biology*, (A. Hollaender, ed.), Vol. I, Part 2, pp. 1145–1201. McGraw-Hill Book Co., New York.

——, A. C. UPTON, K. W. CHRISTENBERRY, W. H. BENEDICT, and J. MOSHMAN. 1954. Some late effects in mice of ionizing radiation from an experimental nuclear detonation. *Radiology*, 63: 562–569.

GARDNER, E. 1940. Decrease in human neurones with age. *Anat. Rec.*, 77: 429–536.

GAULDEN, M. E., and R. P. PERRY. 1958. Influence of the nucleolus on mitosis as revealed by ultraviolet microbeam irradiation. *Proc. Nat. Acad. Sci. Wash.*, 44: 553–559.

GERSH, I., and H. R. CATCHPOLE. 1949. Ground substance and basement membrane. *Amer. J. Anat.*, 85: 457–517.

GETMAN, F. H., and F. DANIELS. 1943. *Outlines of Physical Chemistry*. John Wiley & Sons, New York.

GLÜCKSMANN, A. 1951. Cell deaths in normal vertebrate ontogeny. *Biol. Rev.*, 26: 59–86.

GOMPERTZ, B. 1825. On the nature of the function expressive of the law of human mortality. *Philos. Trans.*, 115 (Series A), 513–589.

GOWEN, J. W. 1959 (in press). Lengthening of life span in mice in relation to two deleterious agents. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

GROSS, J. 1958. Influence of time on the reversible association between large molecules. *Nature, Lond.*, 181: 556.

HAMPERL, H. 1934. Die Fluorescenzmikroskopie menschlicher Gewebe. *Virchows Arch.*, 292: 1–51.

HENSHAW, P., G. STAPLETON, and E. R. RILEY. 1947. The biologic effects of pile radiations. *Radiology*, 49: 349–359.

HOLLAENDER, A. (ed.). 1954. *Radiation Biology.* McGraw-Hill Book Co., New York.

——, and W. D. CLAUS. 1936. The bactericidal effect of ultraviolet radiation on *E. coli* in liquid suspensions. *J. gen. Physiol.*, 19: 753–765.

HURSH, J. B., and G. W. CASARETT. 1959. Recovery from a single dose of X-ray in old and young rats. *Amer. J. Physiol.*, 196: 649–652.

HYDEN, H., and B. LINDSTROM. 1950. Studies on yellow nerve cell pigment. *Disc. Faraday Soc.*, 9: 436–441.

JACOBSON, L. O. 1954. The hematologic effects of ionizing radiation. In *Radiation Biology*, (A. Hollaender, ed.), Vol. I., Part 2, pp. 1029–1090. McGraw-Hill Book Co., New York.

JAYNE, E. P. 1950. Cytochemical studies of age pigments in the human heart. *J. Gerontol.*, 5: 319–325.

JONES, H. B. 1956a. A special consideration of the aging process, disease and life expectancy. *Advanc. biol. med. Phys.* 4: 281–337.

——. 1956b. Demographic consideration of the cancer problem. *Trans. N. Y. Acad. Sci.*, 18: 298–333.

LANDOWNE, M. 1958. The relation between intra-arterial pressure and impact pulse wave velocity with regard to age and arteriosclerosis. *J. Gerontol.*, 13: 153–162.

——, M. BRANDFONBRENNER, and N. W. SHOCK. 1955. The relation of age to certain measures of the performance of the heart and the circulation. *Circulation*, 12: 567–576.

LANSING, A. I. (ed.). 1952. *Problems of Ageing*, 3rd ed. Williams & Wilkins, Baltimore.

MEDAWAR, P. B. 1951. *An Unsolved Problem of Biology.* H. K. Lewis & Co., London. (An inaugural lecture delivered at University College, London).

MILDVAN, A., and B. L. STREHLER. 1959 (in press). A critique of mathematical theories of aging. *J. Gerontol.*

MULLER, H. 1928. The production of mutations by X-rays. *Proc. Nat. Acad. Sci. Wash.*, 14: 714–726.

NORRIS, A. H., N. W. SHOCK, and I. A. WAGMAN. 1953. Age changes in maximum conduction velocity of motor fibers in human ulnar nerves. *J. appl. Physiol.*, 5: 589–593.

PATT, H., and A. BRUES. 1954. The pathological physiology of radiation injury. In *Radiation Biology*, (A. Hollaender, ed.), Vol. I, Part 2, pp. 959–1028. McGraw-Hill Book Co., New York.

PEARL, R. 1928. *The Rate of Living: being an account of some experimental studies on the biology of life duration.* 185 pp. Alfred A. Knopf, New York.

——, and J. R. MINER. 1935. The comparative mortality of certain lower organisms. *Quart. Rev. Biol.*, 10: 60–79.

PUCK, T. T. 1957. The mammalian cell as a microorganism. In *Rhythmic and Synthetic Processes in Growth*, (D. Rudnick, ed.), pp. 3–18. Princeton Univ. Press, Princeton.

SACHER, G. 1955. A comparative analysis of radiation lethality in mammals exposed at constant average intensity for the duration of life. *J. nat. Cancer Inst.*, 15: (4), 1125–1144.

——. 1956. On the statistical nature of mortality with especial reference to chronic radiation. *Radiology*, 67: 250–257.

——. 1959 (in press). Comments. *Proc. Gallinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

SHEPPARD, C. W., and M. STEWART. 1952. The direct effects of radiation on erythrocytes. *J. cell. comp. Physiol.*, 39: (Suppl. 2), 189–215.

SIMMS, H. S., and B. BERG. 1957. Longevity and the onset of lesions in male rats. *J. Gerontol.*, 12: 244–252.

SHOCK, N. W. 1957. Age changes in some physiological processes. *Geriatrics*, 12: 40–48.

——, and M. J. YIENGST. 1952. Basal oxygen consumption and basal respiratory functions in aged males. *J. Gerontol.*, 7: 495.

SINEX, F. M. 1959 (in press). Aging and lability of irreplaceable molecules. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

SOBEL, H., and J. MARMORSTON. 1956. The possible role of the gel-fiber ratio of connective tissue in the aging process. *J. Gerontol.*, 11: 2–7.

STREHLER, B. L. 1958. Symposium on genetic approaches to somatic cell variation. *J. cell. comp. Physiol.*, 52: (Suppl. 1), 317–318.

——. 1959a (in press). Comments. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

——. 1959b (in press). Fluctuating energy demands as determinants of the death process. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

——, D. MARK, A. MILDVAN, and M. GEE. 1959 (in press). Rate and magnitude of age pigment accumulation in the human myocardium. *J. Gerontol.*

——, and A. MILDVAN. 1959 (in press). A general theory of mortality and aging. *Science.*

STÜBEL, H. 1911. Die Fluorescence tierischer Gewebe in ultravioletten Licht. *Pflüg. Arch. ges. Physiol.*, 142: 1–14.

SZILARD, L. 1959. On the nature of the aging process. *Proc. Nat. Acad. Sci. Wash.*, 45: 30–45.

VERZÁR, F. 1955. Veränderung der thermoelastichen Eigenschaften von Sehnenfasern beim Altern. *Experientia*, 11: 230–231.

——. 1959 (in press). Adaptation to environmental

changes in different ages. *Proc. Gatlinburg Conf. biol. Aspects Aging*, 1957. American Institute of Biological Sciences, Washington, D. C.

WEISMANN, A. 1882. *Über die Dauer des Lebens.* Jena, Germany.

WILLIAMS, G. C. 1957. Pleiotropy, natural selection and the evolution of senescence. *Evolution*, 11: 398–411.

YOCKEY, H. 1958. On the role of information theory in mathematical biology. Chap. 11 in *Radiation Biology and Medicine*, pp. 250–282. Addison Wesley Publ. Co., Cambridge, Mass.

NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of Biology. In addition there will occasionally appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to H. B. Glass, Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *Department of Biology, The Johns Hopkins University, Baltimore 18, Maryland, U. S. A.*

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GENERAL BIOLOGY: PHILOSOPHY AND EDUCATION

VALUES IN A UNIVERSE OF CHANCE. *Selected Writings of Charles S. Peirce.*

Edited by Philip P. Weiner. Stanford University Press, Stanford; Doubleday and Company, New York. $3.95 (cloth); $1.25 (paper). xxvi + 446 pp. 1958.

The failure to appreciate in his time the significance of the contributions of Willard Gibbs is often considered the most shameful blot on the history of American intellectual development. It has been equaled, however, by the public neglect in his own day and after of Charles Peirce, probably one of our most influential and certainly one of our most interesting philosophers. He was left for many years to live and to die in penury, and his collected works began to be published only more than ninety years after his birth. Redress for the injury to his person during his lifetime can never be achieved, but perhaps the increasing availability of his works, not only to professional philosophers but also to lay readers, will soon permit his thought to enjoy the high position it merits in history.

The present volume of selections is comprised of a great variety of writings: articles from learned periodicals, from reviews, and from popular magazines; dictionary articles, symposium papers, lectures, letters, unpublished miscellaneous notes, and portions of unpublished manuscripts. A number of these will not be incorporated into the final edition of his collected works. They treat the fields on which he left his strongest mark—pragmatism, over which his spirit still hovers; and the logical theory of signs, which led into later preoccupation with semantics. They deal also with less specialized topics, and present his philosophical views on the historical evolution of thought and on ethical and religious questions. They are written luminously and with wit. An excellent introduction examines some of the origins and influences of his thought, and the notes of the editor throughout the volume could hardly be improved upon. Owners of the collected works will wish to own this volume as a supplement to them, and readers who are not acquainted with Peirce's work at first hand will find it an excellent guide. Peirce deserves a place in hard covers on the shelves of all American philosophers and scientists.

The publishers of Anchor Books are to be congratulated, however, for making the work available to a large population of readers.

JANE OPPENHEIMER

ORIGINE E SVILUPPI DEGLI ORGANISMI. *Alla Luce delle Omologie.*

By Ruggero Verity. Casa Editrice Macri, Firenze. L. 3,800 (paper). xiv + 339 pp.; ill. 1958.

This beautifully printed work is remarkable in proffering a highly synthetic view of organic development and phylogenesis. This view may indeed be rather startling to biologists, who will perhaps not be willing to homologize as freely as the author does between organic and inorganic levels of organization.

The scope and point of view of the work can best be indicated by quoting selected titles from among the 22 chapters that compose it. These chapters are grouped in four parts: Factors of Organization in Inorganic Nature (one chapter); Organic Systems (Chapters 2–13); Morphogenesis (Chapters 14–19); and Phylogenetic Differentiation and Classification (Chapters 20–22).

Under Organic Systems are chapters on: The origin and nature of dynamic organic systems; Organic processes; Organic substances produced in dynamic systems; Differentiations and oscillatory transformations of dynamic systems; Heterotypic divisions in dynamic systems: their cause and the resulting ontogenetic differentiations; Modes of alternating transformation from the anabolic vegetative state to the catabolic dynamic state in the life cycle; and Grades or levels of progressive organization in dynamic systems and the progressive lengthening of their alternating granular and structural stages.

Morphogenesis includes chapters on: Relations between the substances composing the organism and external agents; Differentiation of green plants from saprophytes and animals, and the correspondence of these three types of organism to the three types of cytoplasm (ectoplasm, entoplasm, and mesoplasm); General considerations on the promorphology of the germ cells in multicellular animals.

The last division contains chapters on: Differentiation and phylogenetic separation of organisms; Classification of unicellular organisms in accordance with the rules of development and differentiation; and Relations between the classification of multicellular organisms and the rules of development and differentiation.

The book contains 12 original tables and 16 text figures, most of the latter being adapted from other sources. There is an alphabetical index of terms and definitions.

D. RUDNICK

SCIENCE AND EDUCATION AT THE CROSSROADS. *A View from the Laboratory.*

By Joseph William Still; introduction by Malvina Lindsay. Public Affairs Press, Washington, D. C. $3.75. xii + 140 pp. 1958.

Having caught the contagion of criticism which now plagues the contemporary American educator and scientist, the physician author of this little book has in turn set forth his own (hasty) diagnosis of our educational and scientific health. Unfortunately, the author has chosen to describe and prescribe in a single book for such a rash of symptoms and disorders that no summary of the results of his examination seems possible. It would no doubt be of real benefit to the more discerning reader if, in the current controversy about education, more books were written in which a single problem was examined with leisurely scholarship, and a single thesis developed at sufficient length to be meaningful.

Still's initial, somewhat sanguine assumption is that "education is the basic tool for achieving an end to poverty and disease," and that, based on the development or lack of development of education, and especially upon the spread of scientific information, the prognosis is "One World or None."

In the specific field of education, his panaceas are not really original: "expand and improve," find ways to get and keep enough good teachers, establish national educational standards, increase time spent in school, "end the creed of permissiveness," provide teachers with "solid capitalist rewards," and the like. Some of the author's more specific proposals are worth noting, however. He proposes that research grants be made to institutions and individuals on a long-term basis rather than the present "grant-in-aid-of-projects system." The author, somewhat surprisingly, is opposed to separate education for gifted children—he does not believe that existing psychological tests are a valid basis for such a segregation of students.

One of the more pervasive theses among the multitude of opinions and pronouncements in this book is the author's belief that scientists and teachers have been denied their proportionately just share of rewards (i.e., money and prestige) in a capitalist society. Our current shortage of scientists and teachers would never have occurred, he maintains, if these professions had been properly rewarded. Nevertheless, although the author likens government subsidies and management to dope addiction, and believes them deleterious to the capitalist system, he complains that the basic scientist does not get his fair share of the federal pork barrel.

Lying implacably beneath the currents of this dilemma—a dilemma which the author never resolves—is the stubborn and apparent fact that a free industrial economy is simply too utilitarian to be

concerned with the success or failure of activities which are not immediately productive of material goods. Or, to put the problem differently, what measure shall we use, in a capitalist economy, to evaluate the usefulness of the "pure" scientist and the teacher? Can such an evaluation be justly made on the basis of the laws of supply and demand?

This is essentially a somewhat hasty and superficial book; it is written in a mixture of formal and colloquial styles, and is occasionally marred by confused ideas and confused expressions: e.g., "There are many important *intellectual qualities such as manual skill* [italics added] and creative imagination, which are measured not at all by I.Q.'s or any other kinds of standard tests." Apart from the confusion of ideas in this statement, such a denial of the existence of tests for manual skills is, of course, patently untrue. Although the author has succeeded in sketching a diversity of scientific and educational problems, and in outlining a number of proposed solutions, the current problems in science and education are in need of more probing analyses and more profound solutions than this book presents.

JAMES J. HILL

BIOLOGY: HISTORY AND BIOGRAPHY

BIOGRAPHICAL MEMOIRS. *The National Academy of Sciences. Volume XXX.*

Columbia University Press, New York. $5.00. 409 pp. + 15 pl. 1957.

This volume includes memoirs of Warder Clyde Allee by Karl Patterson Schmidt; of Charles Peter Berkey, by Paul F. Kerr; of George Kimball Burgess, by Lyman J. Briggs and Wallace R. Brode; of Charles Manning Child, by Libbie H. Hyman; of John Dewey, by W. B. Pillsbury; of Enrico Fermi, by Samuel K. Allison; of Bancroft Gherardi, by Oliver E. Buckley; of Frank Rattray Lillie, by B. H. Willier; of Theodore Lyman, by P. W. Bridgman; of George Abram Miller, by H. R. Brahana; of Charles Palache, by Reginald A. Daly; of Lewis John Stadler, by M. M. Rhoades; of Louis Leon Thurstone, by J. P. Guilford; of Alfred Marston Tozzer, by Herbert Joseph Spinden; and of Edward Burr Van Vleck, by Rudolph E. Langer and Mark H. Ingraham.

The birthdates of those remembered fell between 1859 (before the publication of the *Origin of Species*) and 1955; the dates of their deaths between 1932 and 1955. Their average age was 76 at the time they died. Seven were octogenarians or nonogenarians, and two others lived 77 years; thus well over half of the subjects exceeded their three score years and ten. The number of their publications varied from less than thirty to a thousand. Their fields of investigation ranged among Mayan civilization, the embryology of sex, group theory in mathematics, and group behavior in animal aggregations, to mention only a few. One of the scientists described here was studying safety factors in the support of aerial telephone wires in 1900 before the New York Telephone Company was established; another made a key contribution in the 1940's to the development of the atom bomb. One of the biographers begins his notice with the remark that "it is unusual in the lives of scientists to find one man, who, to a considerable degree, has been a pioneer for an era." All of these men have been unique pioneers in a unique era, and the reader of this volume a century hence will be able to say that they were giants in the earth in their time.

JANE OPPENHEIMER

THE MEDICAL WORLD OF THE EIGHTEENTH CENTURY. *By Lester S. King. University of Chicago Press, Chicago.* $5.75. xx + 346 pp.; ill. 1958.

The Medical World of the Eighteenth Century presents a series of 10 separate essays on eighteenth century medicine and pathology. Two of the essays concentrate on the work of a particular individual, Hermann Boerhaave. Others focus on such aspects of eighteenth century medicine as pathology, nosology, homeopathy, and medical ethics. One essay is devoted to a discussion of eighteenth century concepts of fever. Two treat the relative positions in the practice of medicine of the physicians proper as opposed to apothecaries, quacks, and empirics. The final essay, entitled The Practice of Medicine, takes up a number of scattered topics.

The preparation of this book has clearly been a labor of love. Its materials have been collected with diligence and care, and are presented with enthusiasm. It is not completely evident, however, to whom it addresses itself. "The main features of variolation," it says, "are well known." Are they well known to the beginning medical students in whom one wishes to nurture an interest in the history of medicine? "We remember, of course," it says, "that the Renaissance physicians descended from the ecclesiastical practitioner who, hemmed in by church law, could not shed blood." If the book is written for readers who in fact remember this as a matter of course, it should hardly be necessary to labor the points that "to appreciate Boerhaave we must remember the limitations of his knowledge. He knew nothing, for example, about cells in the modern sense. Nor did he have any notion about bacteria or microbiological agents"—and later, "Boerhaave knew nothing about reflex arcs."

I find it difficult to muster up the same degree of approbation for the volume as Ilza Veith expresses in the Foreword. The book is attractively decorated, but even the present reviewer, herself a notoriously poor proofreader, was worried by the number of typographical errors.

JANE OPPENHEIMER

JEWS IN THE WORLD OF SCIENCE.
Edited by Harry Cohen and Itzhak J. Carmin. Monde Publishers, New York. $18.00. xxiv + 263 pp.; ill. 1956.

These biographies are brief and not essentially different from those in standard biographical works. *American Men of Science* probably contains biographies of more Jews than does this volume; one can readily discover unjustifiable omissions, at least in the biological sciences. The price is high, the result not comprehensive, and the quality inferior. The printing in fact resembles mimeographed material. The Preface states the book will satisfy a great need but does not say what; it is indeed difficult to see for what worthwhile use this volume was intended. Of course it makes apparent how very many of our greatest scientists are also Jewish, but one is left to wonder how many also were bald.

DAVID R. EVANS

FRANZ JOSEPH GALL, INVENTOR OF PHRENOLOGY AND HIS COLLECTION. *Wisc. Stud. med. Hist., No. 1.*
By Erwin H. Ackerknecht and Henri V. Vallois; translated from the French by Claire St. Léon; preface by John Z. Bowers. University of Wisconsin Medical School, Madison. $1.50. (paper). 86 pp.; ill. 1956.

ECOLOGY AND NATURAL HISTORY

THE NUMBERS OF MAN AND ANIMALS.
Edited by J. B. Cragg and N. W. Pirie. Published for The Institute of Biology by Oliver & Boyd, London. $2.75. viii + 152 pp. + 1 pl.; text ill. 1957.

In September, 1954, a symposium at the Institute of Biology brought together a group of persons from a variety of disciplines to consider population problems. The lectures and discussions were first published in 1955 and were reprinted in the United States in 1957. On account of the passage of time, it seems suitable to restrict this review to the more lasting contributions. The first 3 lectures consider the optimum human population and the growth of human populations in the world and in an underdeveloped area (Bechuanaland). A chapter of permanent value, by Skellam, discusses the stochastic nature of population growth and points out that extinction is inevitable, since sooner or later random processes lead to a decline to a number below the threshold.

The following four discussions turn to animal populations and consider some ways in which such populations are limited in nature. Almost all of this information has already been published elsewhere. Two chapters deal with problems of human fertility, as might be expected in a book on populations. The final chapters consider the quality of human populations and the future.

From the perspective of 1959 this book lacks cohesion and a purpose. The contents seem routine and lack imaginative synthesis. The quality of individual chapters is high, but it is disappointing that no synthesis or experimental approach has been proposed. The study of human populations will not prosper until a theory, testable by experiments, is formulated.

D. E. DAVIS

ANIMAL ECOLOGY TODAY. *Volume VI.*
By F. S. Bodenheimer. Dr. W. Junk, The Hague. D. G. 28. 276 pp.; ill. 1958.

The reviewer approached this book with pleasant anticipation, for he has long admired Bodenheimer's original contributions. Regrettably, the book was a keen disappointment, for it does not describe ecology as it is today. Indeed, the first chapter, on longevity, includes practically none of the post-war advances in interpretation of data. Chapter III, on the growth of populations, rehashes the old data but includes none of the recent data on the mechanisms responsible for the curve. Similarly, Chapter IV, on biological equilibrium, omits most of the new data on mechanisms of balance.

DAVID E. DAVIS

THE TARANTULA.
By William J. Baerg. University of Kansas Press, Lawrence. $3.00. x + 88 pp.; ill. 1958.

Although this work is concerned with the natural history and behavior of tarantulas in general, the greater part deals with the Arkansas species, *Dugesiella hentzi*, a fact of which we become aware only after reading more than a third of the book. Baerg tells how and where he collected his specimens, and then supplies information on the nature of their food, mating habits, longevity, etc.

There are a number of inconsistencies, such as the statement (p. 12) that tarantulas, when in their burrows, are safe from enemies; yet the author correctly indicates (p. 47) that their chief enemies, the pompilid wasps, nevertheless manage quite successfully to find them in these burrows! Again, we are told

that during feeding "there is not any action [of the jaws] that might be considered chewing or even squeezing"; yet the author correctly indicates that "the grasshopper is reduced [by the tarantula] to a small more or less globular pellet." It is distressing to find teleological statements, such as the following: "the tarantula [after being stung by a wasp] remains alive so as to furnish live meat to the wasp larva." Readers unfamiliar with the details of spider anatomy in general will undoubtedly have a great deal of difficulty interpreting the figures of isolated "mouthparts" and isolated spinners (p. 16–17).

About 10 pages are devoted to a discussion of the venom of tarantulas, and it is perhaps in this field that Baerg is best known. Since Baerg had never known the *quantities* of venom injected by the tarantulas in his various "experiments," contradictions and discrepancies are to be expected. Other workers in this field have pointed out that a tarantula is quite capable of varying the amount of poison ejected.

Probably no American has given more time to the study of these interesting animals than has W. J. Baerg. In this little book he has given us the benefit of some of his experiences, recounted in an informal manner which makes for easy reading.

B. J. KASTON

LES PLUS BEAUX INSECTES.

By A. Villiers. Larousse, Paris. 2,265 fr. 96 pp.; ill. 1958.

This volume of photographs of insects is another of the *Nature et Beauté* series which among others includes volumes on butterflies, birds, mammals, and flowers. Most of the illustrations are close-ups, many are in color, and many are full-page reproductions. Over 100 individual insects are represented, grouped according to order. Emphasis, naturally, is on the more spectacular species. While there are many pictures of live insects in natural surroundings, the collection of the French Natural History Museum has also been used. Since the over-all photography is superb, it is odd that these latter contain disturbing shadows of the insects, which could have been avoided. A brief text in French by A. Villiers discusses the insects represented.

DAVID R. EVANS

THE BIRDS.

By Oskar Heinroth and Katharina Heinroth. The University of Michigan Press, Ann Arbor. $5.00. 181 pp.; ill. 1958.

This little book on bird life was first published under the title *Aus dem Leben der Vögel*, and although we do not possess the original, we assume this to be a verbatim translation. It is concerned with the broad spectrum of bird behavior and ecology and includes such activities as nesting, mating, molting, communication, navigation, and others. Some topics are discussed at greater length (mating and pairing) while others are allotted a simple page (can a bird recognize its own eggs?). Whatever the subject, the long experience of the Heinroths with birds shines through all the pages, and their informal, non-technical style makes it possible for any non-biologist to assimilate the information without difficulty. Readers in this country will appreciate the examples drawn from foreign birds.

HENRI C. SEIBERT

LIVING BIRDS OF THE WORLD.

By E. Thomas Gilliard. Doubleday & Company, Garden City. $12.50. 400 pp.; ill. 1958.

Birds have interested man from earliest times, the first pictures of birds having been painted by Neolithic men in Spanish caves 8000 years ago. Today we are still fascinated by the beauty of birds and their unique patterns of behavior, especially those involving courtship, dress, and motion.

The author, who is Associate Curator of Birds at the American Museum of Natural History, and an authority of the birds of New Guinea, describes in a very lucid and exciting style all groups of birds of the world, and the place of each in the hierarchy of birds.

The general characteristics, structure, relationship, characteristic species, courtship and breeding behavior, number of species, origin and range in the world, and many interesting items of information are given for each family of birds in this popular book. The use of sonar in blind flying, the unique methods of hunting and storing food, the use of objects in courtship ceremonies, the accounts of tool-using among birds, the symbiotic relationships, hibernations, migration, and homing activities, effects of radiation upon birds, and the dangers of extinction are but a few of the many stimulating aspects of bird life discussed.

Over 400 photographs are assembled in this volume. Of these 217 are in color, and vividly display the beautiful and decorative plumage. These illustrations were selected from the works of more than 60 photographers from various countries, and are superbly reproduced in this collection. Most of the birds, including several rare species, have been photographed in their natural habitats. This undoubtedly represents one of the finest collections of bird pictures ever assembled.

SHERWOOD M. REICHARD

COMPARATIVE BIOSYSTEMATICS AND LIFE HISTORY OF THE NUTHATCHES *Sitta pygmaea* AND *Sitta pusilla*. *Univ. Calif. Publ. Zool., Vol. 56, No. 2.*

By Robert A. Norris. University of California Press, Berkeley and Los Angeles. $3.50 (paper). iv + pp. 119–300; ill. 1958.

Sitta pygmaea and *S. pusilla* are two completely disjunct populations of nuthatches, the former found in the western, and the latter in the southeastern part of the United States. Some ornithologists have been impressed by their similarities and have considered them to be one species; others have felt that enough dissimilarity exists for them to be considered as allopatric species. To resolve this question, the systematics, anatomy, life history, ecology, and ethology of the two birds were studied and compared in the field and laboratory. Except for physiological studies, hardly any aspect of bird study has been omitted in this remarkable comparison. An impressive amount of field work has added considerably to our knowledge of these birds. Subtle differences in behavior and structure assume significance when direct comparisons are made and incorporated into the total evidence. For instance, who would otherwise pay attention to the fact that the empty stomach of *S. pygmaea* weighs 0.29 g compared to 0.25 g of *S. pusilla*? Yet when the nature of the food is compared, the difference acquires a meaning that would be lost in a study of only a single species. This publication is recommended to ornithologists and ecologists. At the end, there is no doubt that the weight of the evidence will cause the reader to agree with the writer that these two nuthatches are distinct species.

HENRI C. SEIBERT

WESTERN WONDERLANDS. *A Guide to Bird Habitats of the Western United States.*

By John L. Blackford. Vantage Press, New York, Washington, Hollywood, and Toronto. $5.00. 120 pp. + 96 pl. 1956.

The author has written this habitat guide primarily for the use of amateur ornithologists and field naturalists. *Western Wonderlands* is not intended for use as a manual for identification of birds, but should serve as a most useful supplement to standard bird identification guides. Blackford has covered the principal habitat types found in the area bounded by the Pacific Ocean, the Rocky Mountains, Canada, and Mexico. In all, 18 different habitats are characterized by their plant associations. The checklist of birds for each habitat is divided into three parts: birds which are found at all seasons; those which commonly breed in the particular habitat; and those which occur as seasonal migrants. The addition of specific names would have added to the usefulness of the checklists, which contain only the vernacular names.

The high point of the book is the section of excellent illustrations, consisting of 96 plates of black and white photographs of birds and habitats. The author has made exceptionally good choices of landscapes to illustrate the habitat descriptions in the text. Many of the photographs were taken by the author himself, and all are of superior artistic quality as well as appropriate additions to the material covered in the text.

MARGARET FOREMAN COHN

BIRD WONDERS OF AUSTRALIA.

By Alec H. Chisholm. Michigan State University Press, East Lansing. $5.00. x + 243 pp.; ill. 1958.

This book has been revised and amplified considerably since its first publication in 1934. There are annecdotal descriptions of Birds that Build Playhouses (bower birds), Infants that Commit Murder (cuckoos), and many other groups. In general, the information seems reliable, but it is neither new nor quantitative.

DAVID E. DAVIS

THE BOBCAT OF NORTH AMERICA. *Its History, Life Habits, Economic Status and Control, with List of Currently Recognized Subspecies.*

By Stanley P. Young. The Stackpole Company, Harrisburg and The Wildlife Management Institute, Washington, D. C. $7.50. xvi + 193 pp. + 25 pl.; text ill. 1958.

This book purports to describe the bobcat's history, habits, economic status, and control. It gives in detail the classification from Miller and Kellogg (1955). The information comes largely second or third hand and is uncritically assembled. Apparently the only new data are the analyses of reproductive tracts (by K. L. Duke), showing the breeding in spring. However, persons wishing an enjoyable hour reading about cats will be rewarded.

DAVID E. DAVIS

THE ECOLOGY AND DISTRIBUTION OF THE PSEUDOSCORPIONS OF NORTH-CENTRAL NEW MEXICO. *Univ. N. Mex. Publ. Biol., No. 8.*

By C. Clayton Hoff. University of New Mexico Press, Albuquerque. $1.50 (paper). iv + 72 pp.; ill. 1959.

EVOLUTION

GLACIAL AND PLEISTOCENE GEOLOGY.

By Richard Foster Flint. John Wiley & Sons, New York; Chapman & Hall, London. $12.50. xiii + 533 pp. + 5 pl.; text ill. 1957.

The present volume started out as a revision of the author's *Glacial Geology and the Pleistocene Epoch*, published 10 years earlier, but it has ended up as an entirely new book. This outcome resulted largely from a mass of new data accumulated during the decade, which led to great advances in our understanding of Pleistocene events. These data stemmed particularly from new and rapidly evolving methods of dating, from pollen studies, and from the stratigraphy revealed by sediment cores from ocean floors. In consequence, the extreme upper and extreme lower parts of the Pleistocene series are at present in a state of flux; there is promise, however, that they will become more firm within the very near future.

The most striking differences between the present book and the author's old one involve a new treatment of glaciology intended to be more meaningful in glacial geology, the addition of discussions of sea-floor stratigraphy, soils, frozen-ground phenomena, and geochemical contributions to chronology and the measurement of temperatures. An attempt has been made to present syntheses of Pleistocene animals and plants as well as stratigraphic correlation in greater detail, although the latter poses difficult problems because of its current fluidity.

The approach of this volume remains primarily that of glacial geology, emphasizing the Pleistocene of North America. It is a valuable contribution by one of the leading authorities on the geology of the Pleistocene epoch. Hence, it will be welcomed not only by geologists and paleontologists but also by workers in collateral fields, such as paleoanthropologists, who are eternally faced by the problems of determining the stratigraphic sequence and of dating the remains of fossil man and his forerunners.

WILLIAM L. STRAUS, JR.

EXTINCT AND VANISHING BIRDS OF THE WORLD. *Spec. Publ. No. 13.*

By James C. Greenway, Jr. American Committee for International Wild Life Protection, New York. $5.00. x + 518 pp. + 1 pl.; text ill. 1958.

This scholarly volume is a fitting companion to the book on mammals published in 1942 by Glover M. Allen. A Foreword by Jean Delacour, president of the International Committee, explains that an essential basis for preventing extinction is to understand the current status of threatened species. An introduction states the definition of a species used in the perplexing problems of extinct forms. Then a series of lists give the names and distribution of 44 species and 43 subspecies that are extinct, and of 12 species and 7 subspecies that are probably extinct. In addition, there is mention of hypothetical forms and rare species.

An important section deals with the geography of extinction. The perspective is distorted by the time element; no species in Europe has become extinct for 3 centuries. Presumably, species disappeared when man populated that continent. In contrast, several species have disappeared from North America, but the majority of cases of extinction occur on islands where the introduction of new species of predators, parasites, or man confronted a small population with an unsurmountable problem of rapid adaptation.

The major part of the book describes in detail what is known about each species. The examples present fascinating stories that reflect a thorough examination of the literature. This book merits careful perusal by all biologists interested in the preservation of living things.

DAVID E. DAVIS

TRAITÉ DE PALÉONTOLOGIE. *Tome VI (en deux volumes): Mammifères, Évolution. Deuxième Volume.*

Edited by Jean Piveteau. Masson & Cie., Paris. 16,500 fr. (cloth); 15,500 fr. (paper). viii + 962 pp. + 1 pl.; text ill. 1958.

With the publication of this welcome volume, the end of the great *Traité de Paléontologie* edited by Jean Piveteau is almost in sight. The first 3 volumes, devoted to invertebrates, are already being superseded for American readers, at least, by the more comprehensive *Treatise on Invertebrate Paleontology* under the editorship of R. C. Moore. There is, however, no other modern work on fossil vertebrates of treatise or Handbuch scope, and in this field the *Traité* will be one of the basic references for a long time to come.

As announced, the *Traité* will devote 5 volumes to the vertebrates. Tome IV is to cover the fishes in the broadest sense, and Tome V, already issued, treats amphibians, reptiles, and birds. The last 3 volumes are on mammals and are being published in reverse order. Tome VII, on the primates, has already appeared. Tome VI will treat all the other mammals, in 2 volumes, each of which is a large, separate work. Tome VI, Volume I, not yet issued, will include general matter on mammals, the characteristically Mesozoic orders, and the monotremes, marsupials, cetaceans, carnivores, and artiodactyls. The other orders, 25 in number by the classification adopted, are covered in Tome VI, Volume II, now before us.

Among the major groups from a paleontological point of view (each with 70 or more pages in the *Traité*), R. Lavocat has treated the Notoungulata, C. Dechaseaux and R. Vaufrey the Proboscidea, J. Viret the Perissodactyla, R. Hoffstetter the Xenarthra, S. Schaub the Rodentia, and R. Saban the Insectivora. The groups less numerous as fossils are for the most part divided between Lavocat and

Dechaseaux, with Saban treating the Palaeanodonta and C. Guth the Pholidota. An unusual and useful feature is that for each group where material exists (almost all of the orders) an appended section by Dechaseaux discusses the endocranium. Except for Schaub (Basel, Switzerland) the authors are all French, and all but Schaub and Viret (Lyons) work in Paris. All are highly competent and their close association ensures a fairly unified point of view. There is, however, some reason to regret that wider cooperation was not sought and that this unique, great compendium does not have each group treated by paleontologists, regardless of nationality, who are first-hand authorities on it.

The general coverage is excellent. The student will here find an adequate, clear, and up-to-date characterization of all supergeneric taxa known as fossils. Most genera are named and many are briefly characterized and figured, although no attempt has been made to enable the reader to identify genera from this work alone. The bibliographies are extensive and well selected. The illustrations vary in quality, but they are numerous and almost all are clear. The use of heavy coated paper has permitted good reproduction of both half-tones and line-cuts. The pagination is independent of the rest of the *Traité*, and the volume includes its own index of systematic names.

Close to a thousand tightly organized pages can hardly be criticized in detail in a single review. It goes without saying that no student will agree with all the authors, and that there are some errors. As an example of a difference in judgment on a large scale, the arrangement of the rodents is based on theoretical views as to molar evolution that are questioned by many if not most specialists, and the *Traité*'s approach to that order is not likely to be widely accepted. As another example at a comparatively trivial level, *Endotherium*, here stated flatly to be a Jurassic pantolestid, is probably not Jurassic and surely not a pantolestid. Innumerable such objections can be made against almost any extensive synthesis or compilation. Over all, this one is at least as sound as could reasonably be asked.

The same publisher is simultaneously issuing an even more extensive *Traité de Zoologie*, which includes for each group a summary of known fossils. That treatise includes more than 450 pages on fossil mammals, far less than in the *Traité de Paléontologie* but still making the *Traité de Zoologie* one of the most extensive general modern works on *paleo*mammalogy. The discussions of fossils in the *Traité de Zoologie* are not merely summaries of those in the *Traité de Paléontologie* but are separate studies with some different and even conflicting points. Furthermore, no paleontologist can study a group of fossil mammals without reference to their recent allies, and no neontologist should neglect the extinct and ancestral forms in his group. Thus it is advisable to consult both *Traités* in order to approximate a full review of any group of animals, recent or fossil.

One final, sad remark must be added: both *Traités* are so exceedingly expensive that, among those who need them most, practically no one will be able to buy them. They are not likely to be acquired even by many libraries, especially the smaller libraries where inadequate collections of specialist journals and books make such compendia all the more useful.

GEORGE GAYLORD SIMPSON

VARIATION, RELATIONSHIPS AND EVOLUTION IN THE *PACHYCEPHALA PECTORALIS* SUPERSPECIES (AVES, MUSCICAPIDAE). *Bull. Brit. Mus. (nat. Hist.), Zool., Vol. 4, No. 4.*

By Ian C. J. Galbraith. British Museum (Natural History), London. £1 4s (paper). Pp. 131–222; ill. 1956.

FOSSIL TUBULIDENTATA FROM EAST AFRICA. *Fossil Mammals of Africa, No. 10.*

By D. G. MacInnes. British Museum (Natural History), London. £1 (paper). 38 pp. + 4 pl.; text ill. 1956.

ERINACEIDAE FROM THE MIOCENE OF EAST AFRICA. *Fossil Mammals of Africa, No. 11.*

By P. M. Butler. British Museum (Natural History), London. £2 (paper). 75 pp. + 4 pl.; text ill. 1956.

A NEW MIOCENE RODENT FROM EAST AFRICA. *Fossil Mammals of Africa, No. 12.*

By D. G. MacInnes. British Museum (Natural History), London. £1 (paper). 36 pp. + 1 pl. 1957.

INSECTIVORA AND CHIROPTERA FROM THE MIOCENE ROCKS OF KENYA COLONY. *Fossil Mammals of Africa, No. 13.*

By P. M. Butler and A. Tindell Hopwood. British Museum (Natural History), London. 15s. (paper). iii + 35 pp.; ill. 1957.

TWO ADDITIONAL MIOCENE PORPOISES FROM THE CALVERT CLIFFS MARYLAND. *Proc. U. S. Nat. Mus., Vol. 107.*

By Remington Kellogg. Smithsonian Institution, Washington, D. C. Free upon request (paper). Pp. 279–337 + 30 pl. 1957.

GENETICS AND CYTOLOGY

PRINCIPLES OF GENETICS. *Fifth Edition.*

By Edmund Sinnott, L. C. Dunn, and Theodosius Dobzhansky. McGraw-Hill Book Company, New York, Toronto, and London. $6.75. xvi + 459 pp.; ill. 1958.

This book is probably the most widely used genetics textbook throughout the world. This new and revised edition will therefore be welcomed by everyone concerned with the teaching of genetics. Compared to the fourth edition (*Q.R.B.*, 27: 211. 1952) the present one has a more up-to-date appearance. Reading is facilitated by presentation of the text in two columns. Old figures have been redrawn and are presented in a more modern fashion; various new figures have been added. Whether one prefers certain figures at an angle to the text, like those on pp. 208 and 211, remains a question of personal taste.

Great care has been taken to include recent discoveries and developments in the field. The increasing use of microorganisms for genetic research is duly reflected by added material on the lower fungi, bacteria, and viruses throughout the book. There is a new chapter on sexual reproduction in these lower forms. At the end of the book various recent studies on the fine structure of the genetic material and their bearing on the concept of the gene have been mentioned. The treatment of position alleles, mutational sites within the functional gene, transduction in *Salmonella*, DNA transformation, and the structural organization of DNA are certainly helpful to the understanding of current lines of genetic thought.

This edition also differs from the previous one in that more attention is given to human genetics and the special methods required for studying heredity in man. The increasing exposure of human populations to ionizing radiations necessitates a basic understanding of genetic radiation hazards. In consequence, the chapters on spontaneous and induced mutation have been expanded, and more emphasis has been given to the dynamics of the load of mutations in populations. The part devoted to the genetic effects of radiations on populations would perhaps have been better placed in the general chapter dealing with population genetics than under the heading Crossing, Selfing, Inbreeding, and Heterosis.

In the chapter on induced mutation the text does not always keep pace with more recent findings. The paragraph dealing with the mutagenic effectiveness of neutrons only mentions earlier results on the lower mutagenic effectiveness of this kind of radiation compared to that of x-rays. But a number of more recent studies have shown, that, on the contrary, neutrons are characterized by a greater R.B.E. value. When considering x-ray-induced reverse mutations in *Drosophila*, only Timoféeff-Ressovsky's earlier results and Lefevre's less successful studies are cited, whereas Muller and Oster (1956) have obtained sufficient proof that, as in *Neurospora*, x-rays can produce back mutations in *Drosophila*.

Another new feature of this edition which certainly will prove helpful to the student is the inclusion of a special chapter by Howard Levene on the use of statistics in evaluating genetical data.

Altogether, this new edition of one of the classics in genetics teaching can be expected to be of great help both to instructors and students in this rapidly expanding field.

F. H. SOBELS

FRONTIERS IN CYTOLOGY. *Studies based on a series of lectures presented at Yale University and dedicated to the memory of Henry Bunting.*

Edited by Sanford L. Palay. Yale University Press, New Haven. $9.75. xii + 529 pp. + 254 pl.; text ill. 1958.

This volume of lectures represents a very good cross-section of the current interests of experimental cytologists. The contributions include a brief biography of Bunting, by W. S. Albrink; some current concepts of cellular structure, by E. W. Dempsey; electron microscopic studies of cell surfaces, by D. W. Fawcett; a review by A. R. T. Denues on chromosome structure and function; the effects of purines on tissue culture cells, by J. J. Biesele; the changes in the DNA complex during the mitotic cycle, by D. P. Bloch; the relation of RNA to nuclear and cytoplasmic functions, by J. I. Nurnburger and M. W. Gordon; the histochemistry of intracellular lipids, by H. W. Deane; protein histochemistry, by R. J. Barrnett; the small particulate component of the cytoplasm, by G. E. Palade; the morphology of secretion, by S. L. Palay; the cytology of striated muscle, by H. S. Bennett; the regeneration of striated muscle, by G. C. Godman; pathological swelling and vacuolization of cells, by E. E. Manuelidis; cellular reactions during virus infections, by W. H. Gaylord, Jr.; and the dermal ground substance of the mesenchyme, and collagen and reticulin, by W. G. Banfield. These papers, originally presented in 1956, were brought up to date by the authors in the spring of 1957. Some of them are review articles; others, summaries of the recent work of the authors. It is interesting that, in a work dealing with some of the most fundamental problems of modern cellular biology, almost all of the contributors are affiliated with medical institutions.

Apparently in the interest of economy, 253 figures, including a number of electron micrographs, have been placed at the conclusion of the book. While

these reproductions appear to be of excellent quality, their location is inconvenient and generally discourages consultation at the time when they are referred to in the text. Otherwise, the book is of good quality technically. A bibliography of Buntjing's work is included in Albrink's brief article.

RONALD R. COWDEN

GENERAL AND SYSTEMATIC BOTANY

MARINE ALGAE OF THE NORTHEASTERN COAST OF NORTH AMERICA. *Univ. Mich. Stud., Sci. Ser., Vol. XIII. Second Edition.*

By William Randolph Taylor; illustrated by Chin-Chih Jao. The University of Michigan Press, Ann Arbor. $12.50. viii + 509 pp.; ill. 1957.

It is a pleasure to review a book which is just what its author claims. To compliment W. R. Taylor further on his clear recognition of the limits of his taxonomic floristic manual, one is tempted to comment by quoting from the text itself. However, in brief: the value of taxonomy, as of any other practical art, lies in its usefulness and on that basis one may predict that Taylor's second edition will become highly valued, especially as a manual from which to begin learning about benthic marine algae.

The student working in the text's geographic area and wanting an algal problem will find this book a blessing, for the author points out stretches of coast from which there is little floristic information. Let us hope that students will follow this lead, visit these areas, and publish the results of their findings. Taylor also points out the need for ecological information, another promising area for initial student activity in biology. With this useful taxonomic guide in hand fruitful attacks on such problems will be easier, for the taxonomic work itself will be greatly lessened.

The Preface, setting forth the limits and methods of the work as well as problems yet to be solved, is a useful one. A checklist (pp. 25–32) of the 401 species and 134 subspecific entities, systematically arranged, comes next. The text, which includes dichotomous keys to aid in discrimination between the different taxa from the class down through the species, follows the arrangement of this systematic list. A description accompanies each taxon described; the same splendid plates of figures appear as in the first edition. The bibliography seems to have been extended to include the floristic and pertinent ecological papers that have appeared since the first edition. Finally, one finds the text, but not the plate figures, indexed in a species index.

The nomenclatural code is followed commendably in a conservative manner. Names such as *Laminaria lorea* and *Ceramium areschougii* that had been capitalized in the first edition in line with the Code at that time are now decapitalized. Taylor has replaced the first edition names and citations in the interests of priority or greater precision (e.g., changing "*L. digitata* [L.]Edmonson" of the earlier edition to "*L. digitata* [L.] Lamouroux"). Some familiar names are replaced by names recently demonstrated to be more correct, e.g., *Polysiphonia variegata* and *Polyides rotundus* are replaced, respectively by *P. denudata* and *Polyides caprinus*. Many new algal names appear in this new edition. This is not often, as one might wish, indicative of monographic study, field study or even study of algal material, but rather nomenclatural "discoveries," made largely by the University of California school of thought on such things.

The addition of references to published morphological work is to be commended. Further making this second edition indispensable as a marine algal textbook are useful, otherwise unpublished, notes on techniques for study of the special or classical features of different forms, for example, Taylor's technique for demonstrating the mucilage ducts in the fronds of *Laminaria*.

In comparing the texts of the first and second editions on almost any one of the large common genera one sees at a glance (e.g., in *Laminaria*, again) that Taylor has reconsidered and pursued further the history of many of the species. In this well-known genus, one species (*L. faeroensis* Boerg.) from the previous text has been dropped and two (*L. cuneifolia* J. Ag. and *L. nigripes* J. Ag.) have been added, both of the latter with addition of many new records from the more northern waters. In many cases the basis for what seems to have been an erroneous record is pointed out in footnotes, as in the case of *Alaria*, where several records were based on what seem to have been immature or abnormal specimens. Such situations are often merely stated without reexamination in the treatises of other authors.

One of the sections most completely altered in the new text is that dealing with the Acrochaetiaceae, appearing in the first edition as the Chantransiaceae. Here the current criteria, principally chromatophores, used for segregating the generic entities, have been applied and thus the generic names *Kylinia* and *Audouinella* appear. *Colaconema* appears here too, transferred from its former position in the Bangiales. Many shifts in systematic position appear, as well, among the brown algae. The floristic information and systematic positions are changed, especially, for many of the smaller members of the Phaeophyta. In the Ectocarpales *Giffordia* is introduced as a segregate of *Ectocarpus*, and *Isthmoplea* has been removed to the *Punctariales*. Some of the species earlier included in *Ectocarpus* are found in this edition in such genera as *Hecatonema* and *Streb-*

lomena. Acrothrix is removed from the Desmarestiales to Chordariales.

Another welcomed innovation in this edition is the recognition of *Vaucheria* as representative of a separate class, the Xanthophyceae. One might wish Taylor had introduced a further modern step and treated his classes within phyla, in this case the class Xanthophyceae in the phylum Chrysophyta. The number of species of *Vaucheria* is doubled, due largely to the extensive work on this group in recent years by Taylor himself and his students, A. J. Bernatowicz, John L. Blum, and Townsend Conover.

The recent work distinguishing species of *Enteromorpha* on the basis of living characteristics is not taken up. *E. crinita* is dropped on the opinion that it is but a delicate form of *E. clathrata*. The reason for generally retaining the older treatment of the species is practical usefulness. While genetics and interfertility, the more modern criteria for distinguishing *Enteromorpha* species, may indeed reflect the phylogeny of the species better, or even more truly the species distinctions themselves, specific taxa distinguishable only on such evidence (like carpogonial morphology in the Rhodophyta when only tetrasporic material is at hand) are not of much use to working taxonomists. I believe Taylor's stand in this case, being the more practical, is best for any floristic handbook. The genus *Monostroma* is updated largely by reducing the number of specific taxa to a workable 5 from the obscurely separable 10 of the old text.

All in all, the second edition is a rather thorough revision where practicability was concerned. One might wish that some of the keys had been revised to include more qualitative or quantified discriminations, but perhaps such must await monographic studies of the genera concerned. The author has shown admirable reticence in instances where revision (e.g. in *Enteromorpha*) might have pleased the phylogenetic taxonomist but where it would have made the taxonomy less useful. Additional material extends the 427 pages of the first edition to 509 pages despite the condensation of some of the larger genera. The 82 pages of additional material seem well justified, since now we have a floristic manual that will long be perhaps the most used and useful marine algal flora. It would seem that, despite its cost, the work is nearly an essential for all marine biology students and public libraries near the shores of the Northeastern Atlantic.

MAXWELL S. DOTY

TEXTBOOK OF DENDROLOGY, *Covering the Important Forest Trees of the United States and Canada. Fourth Edition.*

By William M. Harlow and Ellwood S. Harrar. McGraw-Hill Book Company, New York, Toronto, and London. $8.75. xii + 561 pp.; ill. 1958.

The previous, third edition of this widely used forestry textbook was published 8 years ago. In the meantime inevitable changes in nomenclature and classification have been instituted by taxonomists, and an increased knowledge of tree distribution and silvical characteristics has accumulated. As a result, the fourth edition contains numerous revisions of substance. The changes in nomenclature conform in most part to the United States Department of Agriculture's Agriculture Handbook No. 41, the *Check List of Native and Naturalized Trees* (1953). One conspicuous divergence is the retention of the now taxonomically obsolete Latin name *Pseudotsuga taxifolia* (Poir.) Britt. for the Douglas fir (*P. menziesii* (Mirb.) Franco).

For those unfamiliar with this book, it should be noted that it is neither encyclopedic nor local in treatment but is designed primarily to acquaint the student forester with the important forest tree genera of the United States and Canada. Instead of employing detailed taxonomic keys, the distinguishing characteristics of families, genera, and species are presented in tabular form.

SCOTT S. PAULEY

A STUDY OF THE PERENNIAL SPECIES OF *Sidalcea. Part I: Taxonomy; Part II: Chromosome Numbers and Interspecific Hybridizations. Univ. Wash. Publ. Biol., Vol. 18.*

By C. Leo Hitchcock (Pt. I); A. R. Kruckeberg (Pt. II). University of Washington Press, Seattle. $2.00 (paper). vi + 96 pp.; ill. 1957.

MONOGRAPH OF THE GENUS *Russelia* (SCROPHULARIACEAE). *Fieldiana: Bot., Vol. 29, No. 4.*

By Margery C. Carlson. Chicago Natural History Museum, Chicago. $1.50 (paper). ii + pp. 231–292 + 6 pl.; text ill. 1957.

A MONOGRAPH OF THE GENUS *Hydrangea. Proc. Calif. Acad. Sci., Vol. XXIX, No. 5, Fourth Series.*

By Elizabeth McClintock. California Academy of Sciences, San Francisco. $2.00 (paper). Pp. 147–225 + 6 pl.; text ill. 1957.

PLANT MORPHOLOGY AND DEVELOPMENT

PRAKTISCHE EINFÜHRUNG IN DIE PFLANZENMORPHOLOGIE. *Teil II: Die blühende Pflanze.*

By W. Troll. Gustav Fischer Verlag, Jena. DM 26.40. 420 pp.; ill. 1957.

Plant morphology is a subject which belongs both to basic botany and to more advanced studies, and

it is one of the oldest branches of this science and fundamental to many of its approaches. Although it is among the best-known fields of plant study, it is still growing and adding interesting explanations to the general knowledge and understanding of the vegetable kingdom.

Among the many outstanding morphologists of our times, Wilhelm Troll of the University of Mainz is in the leading rank, and his many studies have long been admired and enjoyed by his colleagues from different fields of botany. The same will doubtlessly be true of his very pleasant book on plant morphology, published in two volumes in 1954 (*Q.R.B.*, 31: 137. 1956) and 1957. It is a concentrated account of all phases of the subject, elegantly written with literary citations from the great poet and morphologist Goethe, and filled with photographs and drawings of such quality that they can be expected to find their way into many other textbooks in the years to come.

Professor Troll has divided his treatment in such a way that the first, and smaller, volume describes the morphology of the vegetative parts of the higher plants, whereas the second volume describes the generative parts in the wider sense of the term.

The books are so condensed that even a general description of their approaches and main chapters would not suffice to show their qualities. It may be that a critical morphologist could find several matters of dispute, and it is possible that some of the hypotheses and explanations expressed could be challenged. It might be mentioned that Goethe's explanation of the flower may not be the whole truth, as indicated by some recent anatomical and cytological works. Also, the author is much too authoritative and gives too few references to ideas or explanations other than his own; and in some cases he is even dogmatic. Be this as it may, the books are nevertheless very excellent sources of information for students advancing into special studies in morphology, and also for teachers of the subject who need high-quality manuals for the preparation of their lectures. Although most botany students in America may have difficulties in following Troll's literary, though very exact, language, his books should be available for reference at universities where modern approaches to botany in general, and to plant morphology in particular, are regarded as desirable.

ÁSKELL LÖVE

ORIGIN OF PRIMARY EXTRAXYLARY STEM FIBERS IN DICOTYLEDONS. *Univ. Calif. Publ. Bot., Vol. 30, No. 2.*

By Amélie Blyth. University of California Press, Berkeley and Los Angeles. $1.75 (paper). iv + pp. 145–183 + 23 pl. 1958.

PLANT PHYSIOLOGY

ANNUAL REVIEW OF PLANT PHYSIOLOGY. *Volume 9. Edited by A. S. Crafts; associate editors, Leonard Machlis and John G. Torrey. Annual Reviews, Palo Alto.* $7.00. x + 510 pp.; ill. 1958.

Volume 9 of the *Annual Review of Plant Physiology* begins with a chapter on The Quantum Yield of Photosynthesis by the late, very much-lamented, Robert Emerson. As usual, he has been able to offer adequate explanations for the anomalous observations of Warburg and coworkers, who have found apparent quantum yields indicating extraordinary efficiency in photosynthesis. The last few pages of the article record initial steps in the study of the wave-length dependence of the quantum yield. These studies led directly to the experiments which Emerson performed shortly before his death, and which showed that photosynthesis actually requires (at least under some circumstances) the absorption of light by *both* chlorophyll and an accessory pigment. The review, and the importance of the work described in it, will remain as a testimonial to a career cut short in the middle of a very productive phase.

The Naturally Occurring Auxins and Inhibitors, by J. A. Bentley, and The Destruction of Auxin, by P. M. Ray, both illustrate the increasing difficulties in the way of accepting classical concepts of auxin physiology in toto. Modern methods for analysis find a large number of indole derivatives in plant extracts containing auxin activity; it is certainly not yet possible to tell which forms are transported, which are storage or detoxification products, or which are active in their own right. The products of destruction of indole acetic acid are not fully known, the mechanism for the enzymatic destruction has many controversial aspects, and there is almost no sound evidence on any physiological role for the enzymes that destroy indole acetic acid. Recognition of these deficiencies is certainly the first step toward a clearer understanding in the future.

The review on The Metabolism of Amino Acids and Proteins in Plants, by Yemm and Folkes, is a commendably balanced, up-to-date, and highly organized presentation of nitrogen metabolism. Their article provides the general perspective needed to make the numerous details of nitrogen metabolism coherent. They draw freely on concepts derived from work with bacteria or animals, when it helps them to compose the larger picture. Another article with unusually fine balance and perspective is that on Herbicides by Woodford, Holly, and McCready. It is a pleasure to have assembled in one article the structures and names of the different classes of herbicides now in use. L. Bogorad has a competent review

on the Biogenesis of Flavonoids, reporting the intricacies of their metabolism with admirable aplomb. Material not often reviewed in English is found in the article Morphogenesis in Lower Plants, by L. F. Jaffe. A large part of the work in this area is published in German, and is not often read by American plant physiologists. Although the review is therefore an important one, some sections suffer from a tendency to use undefined terms or to discuss undescribed morphological reactions, so that a reader not very familiar with the biological material is not able to follow the argument. Cytochromes in Plants, reviewed by Lucile Smith and Britton Chance, contains a record of important advances in understanding the functions of these pigments. It is unusual in its full discussion of the problems of methodology in spectrophotometric observations of living tissues, and refreshing in its direct and carefully documented criticisms of the work of Lundegårdh, in particular.

Other articles of considerable interest include: Physiology of the Fresh Water Algae, by R. Krauss (notable for a very inclusive approach, and 467 references); Physiology of Salt Tolerance, by L. Bernstein and H. F. Hayward; Metabolism of Ascorbic Acid in Plants: Part I. Function, by L. W. Mapson; Auxin Uses in the Control of Flowering and Fruiting, by A. C. Leopold; and Postharvest Physiology of Fruits, by R. Ulrich. Much more limited in scope, and of only minor interest, is Mineral Nutrition of Tree Crops, by W. Reuther, T. W. Embleton and, W. W. Jones.

The deplorable custom of including reviews of the physiology of one particular plant is continued in the article Physiology of the Tobacco Plant, by R. A. Steinberg and T. C. Tso. There is nothing in this article that has not been, or could not have been, discussed more appropriately in a larger perspective, in reviews based on some area of plant physiology, or some general principle. The value of the review to plant physiologists in general is almost nil, and represents a waste of space, time, and effort.

A. T. JAGENDORF

RESEARCH IN PHOTOSYNTHESIS. *Papers and discussions presented at the Gatlinburg Conference October 25–29, 1955, sponsored by the Committee on Photobiology of the National Academy of Sciences–National Research Council and supported by the National Science Foundation.*

Edited by H. Gaffron. Interscience Publishers, New York. $12.00. xiv + 524 pp.; ill. 1957.

As the Preface points out, this symposium was organized to facilitate discussion between workers in the various aspects of photosynthesis. Accordingly, the volume contains much of the (often spirited) discussion which followed the 67 papers that are included, a feature which here, as usual, adds much to the report of any symposium. Coverage of the subject is comprehensive except for the deliberate exclusion of any consideration of pathways of carbon reduction and of the minimum number of quanta required. While the book will be useful to many researchers in other areas, the nearly four years which have elapsed since the conference was held (October, 1955) make it a historical report for those actively engaged in photosynthetic research. The contributed papers fall into the following categories: Absorption, fluorescence, luminescence, and photochemistry of pigments in vitro; Absorption, scattering, fluorescence, luminescence, and primary photochemical process in vivo; Possible role of cytochromes; "Dark" reactions; Kinetics, transients, and induction phenomena; and Formation and condition of chlorophyll in the living cell.

DAVID R. EVANS

ECONOMIC BOTANY

THE MUSHROOM HUNTER'S FIELD GUIDE.

By Alexander H. Smith. The University of Michigan Press, Ann Arbor. $4.95. vi + 197 pp.; ill. 1958.

This is a handsome pocket manual for intelligent amateur mushroom hunters in the northern United States. Every description has at least one accompanying photograph in black and white; a total of about 120 mushrooms are described. The emphasis throughout is on careful identification of both edible and poisonous species. The terms used in the descriptions are often cumbersome, since considerable effort has been put into avoiding the technical vocabulary. This aspect may irritate a genuine mycologist, but will be no handicap for the amateur.

The shape of the book is long and narrow, presumably for convenience in carrying. The photographs are all very competent, but lack the glamor of those found in older books on mushrooms, possibly because almost all of them show the mushroom against a neutral screen background rather than in its natural habitat.

A. T. JAGENDORF

INDEX OF AGRICULTURAL RESEARCH, 1957.

Cambridge University Press. $4.00. xiii + 189 pp. 1957.

This list includes almost all of the governmentally financed research on agriculture in the United Kingdom during 1957. A long subject index lists projects according to category. Two smaller indices

follow, which are organized respectively according to animal and crop. Each project is briefly described, and the research organization involved is stated.

FORESTRY TERMINOLOGY. *A Glossary of Technical Terms Used in Forestry. Third Edition.*
Edited by Authur B. Meyer and F. H Eyre. Society of American Foresters, Washington. $3.50. vi + 97 pp. 1958.

Forestry Terminology represents an effort by American foresters to give regional uniformity to those terms used in the many diverse and specialized fields of their profession. Since the technical language of forestry, like any language, utilizes a growing and changing vocabulary, the principal feature of the current edition is the addition of many new terms, chiefly from the fields of forest genetics, aerial photography, and wood utilization. The current edition defines about 4,000 words or phrases. Although the book is a tool of primary usefulness to foresters, it will be found to be a valuable reference for workers in related fields as well.

SCOTT S. PAULEY

GENERAL AND SYSTEMATIC ZOOLOGY

ANIMAL FORM AND FUNCTION. *An Introduction to College Zoology. Second Edition.*
By W. R. Breneman. Ginn & Company, Boston, Dallas, New York, Palo Alto, Chicago, Toronto, Atlanta, and London. $7.75. xii + 595 pp.; ill. 1959.

Any reviewer's commentary on the selection of a general zoology text is bound to reflect his own bias. This is particularly the case when the book departs to some degree from established tradition. In this textbook the author has attempted to relate form and function in the animal kingdom in a way meaningful to the student. In the Preface, readers are informed that the presentation of ecology, embryology, genetics, and other areas of biology, has been purposely restricted to what the student could be reasonably expected to understand in the light of his accumulated knowledge of animal biology. The presentation of each section, however, probes deeply into the functional aspects of structure, even to the submicroscopic and macromolecular level. In this way the student is to be made aware of problems in modern biology and prepared in many ways for the subsequent study of these problems in greater detail.

It has been assumed, and rightly, that a student of zoology should devote his first year simply to learning about animals. There are many fine illustrations, and there is an adequate reading list at the end of each chapter. Each chapter has a catchy title: A Biological Success Story: Phylum Arthropoda; or, How to Live on Income: Parasitism. Ample evidence of the author's humor underlines the fact that studying biology can really be great fun.

While the orientation of this textbook may not sit well with instructors who like to rush first-year biology students into an acquaintance with "frontier problems," it will probably please those who council restraint, a more classical approach, and yet who want to prepare their students for courses in experimental biology later.

RONALD R. COWDEN

BEITRÄGE ZUR NEOTROPISCHEN FAUNA. *Band 1, Heft 1. Edited by Erich Titschack and Hans-Wilhelm Koepcke. Gustav Fischer Verlag, Jena.* DM 10 (paper). Pp. 1–68; ill. 1956.

THE INVERTEBRATA. *A Manual for the Use of Students. Third Edition.*
By the late L. A. Borradaile and F. A. Potts, with chapters by L. E. S. Eastham and J. T. Saunders; revised by G. A. Kerkut. Cambridge University Press, New York. $8.50. xviii + 795 pp.; ill. 1958.

Zoologists will be pleased to see this veteran textbook rejuvenated, by the addition of much new material and the revision of the old. Especially is this true of such scientifically and economically important groups as the insects, nematodes, and mollusks. The coverage of regeneration and development has been increased, and the classes and orders of each phylum are now clearly set forth in bold type near the beginning of each chapter. The higher reaches of the animal kingdom have been grouped into the annelid-mollusk-arthropod (Protostome) branch and the echinoderm-chordate, (Deuterostome) branch. The text figures are far easier to follow because the labels are placed on the figures, so that it is no longer necessary to hunt through the captions to discover what, for example, *ep. i.* or *np. q.* mean. The total number of figures has been increased by 40 (not by 100, as the publisher's statement on the jacket implies). An extremely useful annotated bibliography, organized by general topics and by chapters, is an entirely new feature.

The adverse criticisms of such a revision fall into two categories. The first includes matters of opinion. Any author of such a volume is forced to make many hard choices. Personally, I would have included at least some material on the endocrine structures controlling insect metamorphosis, even if it meant short-changing insect paleontology. It seems surprising

that the newer view about the origin of the Metazoa from the multinucleate ciliates through the acoelous flatworms is mentioned only in a single sentence, and that neither of its originators, Sedgwick and Hadzi, is named. This is all the more surprising because the theory has been extensively discussed and much evidence bearing upon it presented by prominent British zoologists.

The second category includes obvious oversights and errors. My old copy of Borradaile and Potts, which I have treasured since 1936, presented a fascinating discussion of "senescence" in ciliates and its cure by the mythical process of "endomixis," illustrated by a figure "From Robertson after Jennings." In the present 1958 edition there is the same discussion of senescence and endomixis, identical word for word, paragraph after paragraph, and illustrated by the same "From Robertson after Jennings" figure of "endomixis." Yet genuine mating types are not so much as mentioned. The treatment of the coelenterates as a whole follows Haeckel and does not suggest even the possibility of any other view, despite the sharp words and cogent evidence of their essentially triploblastic nature given by Hyman in the first volume of her series, and despite the work of Hadzi and others. Surely the student should be informed that other views than Haeckel's exist. Although the bibliographies in general are well chosen and up to date, both Tinbergen and Lorenz are omitted from the list on animal behavior, and, for North American use, the list on identification should have included both H. S. Pratt's *Manual of the Common Invertebrate Animals* and R. W. Pennak's *Freshwater Invertebrates*.

GAIRDNER B. MOMENT

PELAGIC POLYCHAETES OF THE PACIFIC OCEAN. *Bull. Scripps Instn. Oceanogr. tech., Vol. 7, No. 2.*

By R. Phillips Dales. University of California Press, Berkeley and Los Angeles. $3.00 (paper). iv + pp. 99–167; ill. 1957.

PACIFIC SEA SHELLS. *A Handbook of Common Marine Molluscs of Hawaii and the South Seas. Revised Edition.*

By Spencer Wilkie Tinker. Charles E. Tuttle Company, Rutland and Tokyo. $3.25. 240 pp.; ill. 1958.

This is a popularization for beginners of the study of univalve mollusks of the central part of the Pacific Ocean. The bivalves have been omitted because, in the words of the author, they are not interesting. What a misunderstanding! Any one who really knows the bivalves will find them just as interesting as the gastropods. Their omission is as unfortunate as it is misleading.

It is of course quite impossible to treat all the gastropods of the mid-Pacific islands in a single book, especially in a book limited to 250 pages. A selection must be made. In the present case, the reader is likely to wonder why, if the book was written primarily to enable the beginner to identify his finds, so many species have been included of whose identity the author himself is uncertain, so that he cannot cite more than the generic name.

Another peculiarity of this work is the tendency to figure the shell with the spires pointed downward. This is in fact logical, because the spire in life projects posteriorly. But why then should an exception be made of the genus *Conus*, all the species of which are figured with the spire pointing upward?

The science of conchology is now undergoing a renascence of popularity, evident from the formation of conchological clubs all over the country, even in inland continental localities, far from the sea coast. Beginners' books are badly needed, and this one is likely to meet a certain demand. The index is very complete; it covers 8 pages, or about three per cent of the book.

JOSHUA L. BAILY, JR.

GENERAL AND APPLIED ENTOMOLOGY.

By V. A. Little. Harper & Brothers, New York. $7.00. x + 543 pp.; ill. 1957.

The Preface states that this text is written for the beginning student in the science of entomology. The author seems to assume that it is also the student's first exposure to the science of biology, as he takes the trouble to define such terms as phylum and class and to discuss briefly the kinds of organisms found in the principal ones. The need for such elementary introductory material clearly indicates a trend in this country in the teaching of entomology which needs serious reevaluation. Many professional entomologists are being trained much too narrowly, and it has become quite clear that there is a definite lack of understanding of basic biological principles among many of those recently trained in this specialized field of biology. The failure to impart these principles could easily be rectified by adding a requirement of at least two years of introductory work in basic biology before a student advances to courses in his professional field.

The first part of this textbook deals with general topics. Fourteen chapters are devoted to a more detailed treatment of the orders of insects. Where certain forms are economically important, the author suggests methods of control. There are also 2 chapters on insecticides and insect control. The book is thoroughly illustrated to show examples of various kinds of insects, with emphasis directed toward those of economic importance. The final chapter intro-

duces the student to the subject of collecting, mounting, and preserving insects.

Although the textbook may meet the requirements of many entomology departments, it does not offer the challenge to the student's ability that is so sorely needed in the continued upgrading of this field in the United States.

LEWIS BERNER

ANNUAL REVIEW OF ENTOMOLOGY. *Volume 4.*

Edited by Edward A. Steinhaus; associate editor, Ray F. Smith. Annual Reviews, Palo Alto. $7.00. viii + 467 pp.; ill. 1959.

This fourth volume of the series contains a slightly greater proportion of reviews of basic research than some of the earlier ones. Especially interesting is the article by Karlson and Butenandt on ectohormones, which have proven to be so important in the sexual, developmental, and social relations of insects. The review of Baerends reflects the increasing recognition of ethology by American researchers. Day and Grace summarize the timely topic and difficult problem of the culture of insect cells in vitro. There are, in addition, the following: Insect blood cells (Wigglesworth); Insect pigments (Cromartie); Taxonomic problems with closely related species (Brown); Ecology of Cerambycidae (Linsley); Biology of aphids (Kennedy and Stroyan); Biology of parasitic Hymenoptera (Doutt); Bioclimatic studies with insects (Messenger); Experimental host-parasite populations (Burnett); Biological control of weeds with insects (Huffaker); Microbial control of insect pests (Tanada); On the mode of action of insecticides (Winteringham and Lewis); Biological assay of insecticide residues (Nagasawa); Deciduous fruit insects and their control (Barnes); Seed treatment as a method of insect control (Lange); Fleas and disease (Jellison); and Insects and the epidemiology of malaria (Russell).

DAVID R. EVANS

THE GRASSHOPPERS AND LOCUSTS (ACRIDOIDEA) OF AUSTRALIA. *Volume 3.*

By James A. G. Rehn. Commonwealth Scientific and Industrial Research Organization, Melbourne. £2. 273 pp. + 29 pl. 1957.

This is the third volume of a systematic work on the grasshoppers of Australia, based in the main on the material in the collection of the Division of Entomology of the Commonwealth Scientific and Industrial Research Organization. The work is very well illustrated, with 16 plates of photographs and 12 of drawings (402 individual illustrations). The descriptions of the species are extremely detailed, in fact unnecessarily so, it would seem. A total of 33 species are dealt with in this volume of the series, of which 15 are described as new.

The Asiatic and African tribe Oxyini is represented in Australia by a number of hygrophilous tropical and subtropical species, only one of which extends into the temperate areas of eastern Australia; the genera *Oxya* and *Gesonula*, each with a single species in Australia, undoubtedly represent relatively recent arrivals from New Guinea, but *Bermius* and *Tolgadia*, each with several species, are endemic genera of the Oxyini. The Praxibulini are entirely endemic to Australia. The general reader will be interested within this tribe in the genus *Kosciuscola*, high-mountain grasshoppers which exhibit a unique temperature-controlled physiological color change (Key and Day, *Austral. J. Zool.* 2: 309–363). Some members of this genus (and also of the related genus *Praxibulus*) exhibit a striking "feminization" of males following parasitization by nematodes. The species *Praxibulus insolens* Rehn in the present work has most likely been established on parasitized individuals of the common *P. laminatus* (Stål).

M. J. D. WHITE

THE ANTS.

By Wilhelm Goetsch. University of Michigan Press, Ann Arbor. $4.50. 169 pp.; ill. 1957.

This attractive little book is a general treatment of the subject designed for the layman. It is eminently readable, and the illustrations are clear and mostly useful (some are borrowed without credit). Nevertheless, it has serious shortcomings.

First it is padded as a result of the classical format. A page of conventional size (6 x 9 inches) would not only have allowed longer lines but would have permitted printing alongside the narrow figures; many of these spaces are left blank. The bottom margin is too wide; two more lines could have been accommodated. The outer margins are wider than necessary, while the gutter is too narrow for convenience. But then, if space had been economized, the volume would probably have been too thin to bind in hard covers. The paper has a glossy finish which reflects an unpleasant glare. This enameled stock is hardly justified by the 4 photographs, for they might just as well have been omitted.

Then there are a number of outright errors. Just as bad are the many quasi-errors—words or statements which, although not literally wrong, are nevertheless likely to mislead or confuse the reader. The latter may be the result of translation from the German by someone not familiar with myrmecological usage.

Treatment of the brood is limited to half a page, which is strange considering the importance of the

young animal societies. Behavior receives a disproportionately large share of the book, presumably because this is the author's specialty. The treatment is free of anthropomorphism. In spite of the author's warning that his descriptions of behavior concern particular species, the reader nevertheless gets an impression that they apply to ants in general.

With all its faults the book is still recommended to any layman who will skip the first 40 pages. On the whole, it is rather good, but it could have been so much better had it been edited by an English-speaking myrmecologist.

GEORGE C. WHEELER

CONTRIBUTIONS TOWARD A RECLASSIFICATION OF THE FORMICIDAE. II. TRIBE ECTATOMMINI (HYMENOPTERA). *Bull. Mus. comp. Zool. Harv., Vol. 118, No. 5.*

By William L. Brown, Jr. Museum of Comparative Zoology at Harvard College, Cambridge. $1.90 (paper). ii + pp. 175–362; ill. 1958.

Although the author still calls it Ectatommini, the tribe bears scant resemblance to that one of the same name in Emery's *Genera Insectorum* (1911). The former tribes (of the subfamily Ponerinae) Ectatommini, Paraponerini, and Proceratiini have here been combined, after the exclusion of 4 genera. The remaining 29 genera and subgenera have been reduced by synonymizing to 9 genera: *Acanthoponera, Aulocopone, Discothyrea, Ectatomma, Gnamptogenys, Heteroponera, Paraponera, Proceratium,* and *Rhytidoponere*. There are no subgenera, subspecies, or varieties. Nineteen new species are described.

GEORGE C. WHEELER

THE NORTH AMERICAN SAWFLIES OF THE GENERA *Acantholyda, Cephalcia,* AND *Neurotoma* (Hymenoptera, Pamphiliidae). *Univ. Calif. Publ. Ent., Vol. 14, No. 2.*

By Woodrow W. Middlekauff. University of California, Berkeley and Los Angeles. $2.50 (paper). iv + pp. 51–168 + 3 pl.; text ill. 1958.

This report provides an excellent classification of the Nearctic species of the sawfly family *Pamphiliidae* except for the genus *Pamphilius*, for which a forthcoming revision is planned by Middlekauff. This family is of unusual interest because it is one of the truly archaic families in the insect order Hymenoptera. Introductory sections of this paper give interesting material on the history, external morphology, phylogeny, and geographic distribution, and bionomics, as well as the classification, so as to present a well-rounded introduction to the study of the family. Several new and welcome characters which are diagnostic of the various genera are illustrated for parts of the head, legs, and genitalia. The section of classification treats 3 genera comprising 48 species, of which 11 are new to science. Excellent keys are provided for identification of the species, and treatments of the individual species provide adequate descriptions and detailed distribution records. A distinctive feature of the paper is the large number of illustrations of the intricate color patterns exhibited especially on the heads of these sawflies, characters which are difficult to describe and which, in many cases, provide excellent diagnoses. This paper is a most valuable addition to a knowledge of the North American sawfly fauna, since it treats a group long neglected. It will be highly useful for many years to come.

HERBERT H. ROSS

CATALOGUE COMMENTÉ DES COLÉOPTÈRES DU MAROC. *Fasc. II, Hydrocanthares, Palpicornes, Brachelytres. Trav. Inst. sci. Chérif., Sér. Zool., No. 14.*

By Louis Kocher. Société des sciences naturelles et physiques du Maroc, Rabat. 840 fr. (paper). 244 pp. 1958.

CATALOGUE COMMENTÉ DES COLÉOPTÈRES DU MAROC. *Fasc. VI, Tenebrionides. Trav. Inst. sci. Chérif., Sér. Zool., No. 12.*

By Louis Kocher. Société des sciences naturelles et physiques du Maroc, Rabat. 640 fr. (paper). 185 pp. 1958.

Two parts of the extensive catalog of the beetles of Morocco of which Parts 3, 4, 5, and 8 have appeared previously. The catalogue contains a systematic listing of all species found in Morocco (843 species in Part II, 711 species in Part VI). There are records of specific locations, comments on older records, occasional taxonomic notes, etc.

For the Tenebrionidae the author has taken into account the fact that numerous races exist in Morocco because of long isolation, since these insects are generally unable to fly. The exact status of many of these forms is uncertain and presents serious problems of identification which can only be solved with local knowledge.

The appearance of this catalog renders the distribution of beetles in Morocco better known than in many, more easily accessible countries.

G. H. DIEKE

CATALOGUE COMMENTÉ DES COLÉOPTÈRES DU MAROC. *Fasc. VII, Lamellicornes. Trav. Inst. sci. Chérif., Sér. Zool., No. 16.*

By Louis Kocher. Société des sciences naturelles et physiques du Maroc, Rabat. 360 fr. (paper). iv + pp. 7–83. 1958.

A REVISION OF THE SPECIES OF *Pandeleteius* SCHÖNHERR AND *Pandeleteinus* CHAMPION OF AMERICA NORTH OF MEXICO (COLEOPTERA: CURCULIONIDAE). *Proc. Calif. Acad. Sci., Vol. XXIX, No. 10. Fourth Series.*

By Anne T. Howden. California Academy of Sciences, San Francisco. $1.50 (paper). Pp. 361–421 + 2 pl. 1959.

THE FRESHWATER FISHES. *Pictured-Key Nature Series.*

By Samuel Eddy. William C. Brown Company, Dubuque. $3.25; $2.75 (spiral bound). 253 pp.; ill. 1957.

This book bears the inclusive subtitle, *Pictured-Keys for Identifying All of the Freshwater Fishes of the United States and Also Including a Number of Marine Species Which Often Enter Freshwater.* Writing a thoroughly reliable manual for the identification of all the freshwater fishes of the United States would be an almost impossible task, particularly at a time when a vast amount of information has been gathered but only partly presented in the widely scattered literature—and at a time when much remains to be done, even in the initial description of species. The several attempts that have been made over the past three decades to meet this need have all fallen far short of perfection. Eddy's courageous try was an improvement in some respects, particularly in the extensive illustrations. These pen-and-ink sketches by the author, though crude in fin structure, are, as a rule, highly characteristic in form, squamation, and coloration. Many species are here figured for the first time. A generally successful effort was made to bring information up to date. The main aim was obviously to provide for the ready and correct determinations of species, without regard to relationships or to a full outline of diagnostic characters. The effort was moderately successful, though the arrangement yields some strange bedfellows, and the paucity of characters will lead at times to erroneous identifications. For serious purposes, identifications made with such a manual should be followed by reference to more technical works, or by submission of samples to specialists. This is particularly true for species from the western regions, for which the inevitable minor errors are most numerous. Errors, as in distribution, are also numerous for the southeastern regions. Furthermore, significant identification often involves subspecies, which are almost consistently excluded from consideration in this attractive manual.

CARL L. HUBBS

THE FISHES OF OHIO.

By Milton B. Trautman; illustrated by the author. The Ohio State University Press, Columbus. $6.50. xviii + 683 pp. + 7 pl.; text ill. 1957.

This abundantly documented and profusely illustrated treatise brought to gratifying fruition nearly a third of a century of almost ceaseless labor by an enthusiastic and able field naturalist, following nearly as long a period of previous work by others. It was the long-delayed product of a perfectionist. Every stream of any consequence was sampled from source to mouth: the almost evenly stippled map of collecting stations illustrates the most thorough survey ever made of the freshwater fishes of a like area. All available previous material as well as all published information was scrutinized. Problems that arose were worked and reworked. The final product abundantly reflects the effort and work that went into it.

As a manual for identification the treatise is a model. Methods and glossary are detailed. The keys to families are adequate and the keys to species and subspecies are thorough, well-tested, meticulous, and usefully illustrated. The pen-and-ink illustrations of each form are precise representations of average specimens, often with inserts showing anatomical features, characters of the young, breeding tubercles, etc. Diagnostic features are emphasized. The book will be useful as a manual throughout much of eastern North America.

This state fish book is, however, much more than a manual: it is a scholarly contribution to ichthyology, ecology, and biogeography. It excels in the interpretation of the past and present distributions of Ohio fishes in terms of Glacial events, physiography (notably stream gradients), and the tragic modifications of habitat by man. The background for these interpretations is given in introductory sections; the actual data on the fishes are largely confined to the accounts of the individual species. Here can be found a wealth of information on regions and habitats now selected and on past changes in distribution. Trautman has proved himself to be a keen observer, an able ecologist, and a capable historian. The distribution of each form is indicated, by all record stations, on a separate map. These maps show the complete drainage base, often supply distinctive symbols for early and recent records, and often indicate physiographic boundaries or areas. An insert on each map shows, with somewhat less precision, the general distribution of each form.

Twenty-one species are splendidly presented on 7 original color plates. What a pity it is that more species cannot be so illustrated in works of this sort! This large and magnificent volume must have been very heavily subsidized to allow it to be purchased at a price that today is so surprisingly modest.

CARL L. HUBBS

GUIDE TO THE FISHES OF NEW MEXICO.

By William J. Koster. University of New Mexico Press, Albuquerque. $1.00 (paper). vii + 116 pp.; ill. 1957.

This is announced as a preliminary account of the fishes of New Mexico, published pending the completion of a detailed study in preparation by the author. The present publication is indicated as intended for popular use, and is undocumented. The text, nevertheless, reflects a very considerable amount of collecting, study, and consultation. Prior to Koster's studies, the fish fauna of New Mexico was very inadequately elucidated. The work done there over the last third of a century by the staff of the University of Michigan Museum of Zoology unfortunately remains largely unpublished. In the initial section on the distribution of fishes Koster mentions the high probability, long recognized but not adequately presented by the Michigan group, that the fauna of the upper Pecos River was derived by stream capture from that of the Canadian River of the Mississippi drainage basin; but he does not point out that this Mississippian fauna of the upper Pecos is more or less segregated from the Rio Grande fauna by the high salt content of the middle Pecos. The introduction, on the biology, management, and study of fishes, covers only 13 pages, but contains a considerable amount of sound information. The main text embodies general remarks on the fishes of each family, followed by well-selected and reliable statements on the characters and life-ways of the individual species. Subspecies, unfortunately, are left untreated. Considering the great limitations of simple outline drawings, in which a few streaks represent the soft rays, the illustrations (prepared by the author from his photographs) are surprisingly characteristic.

CARL L. HUBBS

THE BIOLOGY AND SYSTEMATICS OF THE PINFISH, *Lagadon rhomboides* (LINNAEUS). *Bull. Fla. Mus. Biol. Sci., Vol. 2, No. 6.*

By David K. Caldwell. University of Florida, Gainesville. $1.25 (paper). Pp. 78–173; ill. 1957.

VARIATION AND SYSTEMATIC RELATIONSHIPS WITHIN THE SALAMANDER GENUS *Taricha. Univ. Calif. Publ. Zool., Vol. 56, No. 3.*

By William J. Riemer. University of California Press, Berkeley and Los Angeles. $2.00 (paper). iv + pp. 301–390; ill. 1958.

REVISION OF FIVE AFRICAN SNAKE GENERA. *Bull. Mus. comp. Zool., Harv., Vol. 119, No. 1.*

By Arthur Loveridge. Museum of Comparative Zoology, Cambridge. $2.40 (paper). 198 pp. 1958.

The snakes of continental Africa are here assigned to approximately 90 genera distributed among 6 families. However, no fewer than 66 of these genera belong to a single family, the Colubridae. As the largest, most widely represented, and most diversified group of snakes, this family inevitably poses more problems for the systematist than any other. Africa has been an important subcenter in the evolution and differentiation of the group, as indicated by the fact that all but 9 of the 66 genera are restricted to that continent. The Sahara appears to serve as the barrier restricting the dispersal of all but 2 of 59 genera that probably evolved in Africa.

Since 1919 much of our knowledge concerning East African snakes can be traced to the pen of Arthur Loveridge, who recently retired after completing this meticulous revision of 5 colubrid genera, *Lycodonomorphus, Natriciteres, Philothamnus, Prosymna,* and *Chilorhinophis*. With Madison Avenue influences not otherwise apparent, Loveridge describes this work as an attempt to "synopsize" all pertinent information concerning the 27 species included in the 5 genera. Definitions of each genus are followed by keys, tables, and brief descriptions for the identification of species and subspecies. Supplementary information appears under such headings as habitat, diet, parasites, enemies, and range, with exhaustive lists of localities.

These revisions could have been greatly enhanced by the inclusion of illustrations or the use of distributional maps. Nevertheless, Loveridge's summary of data obtained from the material he examined and his critical appraisal of information derived from 345 sources cited in the bibliography make this an important contribution.

CHARLES M. BOGERT

GEORGIA BIRDS.

By Thomas D. Burleigh; reproductions of original paintings by George Miksch Sutton. University of Oklahoma Press, Norman. $12.50. xxx + 746 pp. + 35 pl.; text ill. 1958.

In most respects this volume is a conventional "state bird book." For each species it delimits the distribution, indicates the status in Georgia, and describes the habits. Only rarely does new or quantitative information appear. Two introductory chapters are provided. One, by William W. Griffin, relates the history of ornithology in Georgia; the other, by Robert A. Norris, is a splendid account of the physiographic regions in the largest state east of the Mississippi. This chapter is a source of information, applicable also to adjoining states, that illuminates the distribution of birds. The 35 colored plates illustrate many species, but their reproduction is poor; the colors are not true, and the paper seems unsatisfactory.

DAVID E. DAVIS

DISTRIBUTIONAL CHECK-LIST OF THE BIRDS OF MEXICO. *Pacific Coast Avifauna No. 33. Parts 1 and 2.*

(Part 1) Cooper Ornithological Club, Berkeley; (Part 2) Cooper Ornithological Society, Berkeley. $9.00. (Part 1) 202 pp.; (Part 2) 436 pp.; ill. (Part 1) 1950; (Part 2) 1957.

The two parts of the list are bound together into one volume. The information includes taxonomic status and range.

CONTRIBUTIONS TO THE ORNITHOLOGY OF WESTERN SOUTH AFRICA. *Results of the Brit. Mus. (nat. Hist.) South West Africa Expedition, 1949–50.*

By J. D. MacDonald. Trustees of the British Museum, London. £1 15s. xi + 174 pp. + 7 pl.; text ill. 1957.

The west coast of South Africa is a desolate, arid, sparsely inhabited stretch of wasteland whose avifauna is less well known than that of most other parts of Africa. A bird-collecting expedition, lasting for 4½ months, started from Cape Town and traveled north to Onguati and Kamanjab (20° S). The results of this trip are reported in this publication. Whereas the notes on the species collected are primarily of interest to the ornithologist, the short but excellent review of the physiography, soil, climate, and vegetation of the region makes this book valuable to the ecologist as well. There are also valuable discussions of the effects of physiography and climate on speciation and distribution, on the relationship of plumage color to soils and vegetation, and on variations in the breeding season.

HENRI C. SEIBERT

BIRDS FROM NEPAL. *Fieldiana: Zool., Vol. 41, No. 1.*

By Austin L. Rand and Robert L. Fleming. Chicago Natural History Museum, Chicago. $3.50 (paper). 218 pp. 1957.

The systematic list contains 490 species and subspecies of birds collected during a series of expeditions to various parts of Nepal. The itinerary of each trip is carefully outlined. This report is mostly taxonomic and distributional, and supplies very little information about the country, except as mentioned in the itinerary, or about the ecology of the birds. It does, however, add significantly to our knowledge of birds from an interesting region of the world.

HENRI C. SEIBERT

THE BROWN SKUA *Catharacra skua* LÖNNBERGI (MATHEWS) OF SOUTH GEORGIA. *Falkland Islands Dependencies Survey; Scientific Reports, No. 14.*

By Bernard Stonehouse. Her Majesty's Stationery Office, London. 10s. (paper). 25 pp. + 2 pl.; text ill. 1956.

LES MAMMIFÈRES. *Primates, Carnivores, Pinnipedes, Artiodactyles. Trav. Inst. Sci. Chérifien, Sér. Zool., No. 5.*

By Jean B. Panouse. Société des sciences naturelles et physiques du Maroc, Rabat. 1,900 fr. (paper). 212 pp. + 11 pl.; text ill. 1957.

This book is the second in a series on the mammals of this country of the Palaearctic portion of Northwest Africa. The first volume dealt with the bats. Presumably at least one subsequent volume will cover the rodents and other orders.

The book is little more than a checklist and identification manual. There are simple dichotomous keys to the orders and families, and, within each group, keys to species. For some species there are good distribution maps, but these are not by any means provided for all. For each species there is given its proper bi- or tri-nomen, a brief description of its appearance, its measurements, and its cranial characters. There follows a discussion of its biology and distribution. The amount of information encompassed in the latter naturally varies greatly. For a considerable number of species there are good line drawings to illustrate the characteristics of the skull.

Lion, elephant, hartebeest, addax, and oryx are the larger mammals listed as formerly having occurred in Morocco, but no longer to be found there. The leopard and cheetah are the only large cats remaining, and the latter is extremely rare.

There are 11 plates, 10 in color, at the end of the book. Some are obviously of stuffed museum specimens, others were taken in zoos. A few may be from life. The color reproduction is good, and most of the carnivores and ungulates are represented, as there are two illustrations per plate. As is usual with French publications, the book has a very insubstantial binding.

BRYAN P. GLASS

THE GREAT ANTILLEAN INSECTIVORES. *Bull. Amer. Mus. nat. Hist., Vol. 115, Art. 3.*

By Samuel Booker McDowell, Jr. American Museum of Natural History, New York. $1.75 (paper). iv + pp. 117–214; ill. 1958.

HAIR STRUCTURE AS A GENERIC CHARACTER IN BATS. *Vol. 59, No. 8.*

By Frances A. Benedict. University of California Press, Berkeley and Los Angeles. $4.00 (paper). iv + 528 pp. + 32 pl. 1957.

Since 1920, when Hausman published his first paper on the subject, the structure of hair has received considerable attention as a tool in mammalian taxonomy. Miss Benedict has been able to apply this approach to the study of intra-ordinal relationships between the families and genera of bats with con-

siderable success, so much so that it has been possible to devise dichotomous keys for the identification of bats to the family and in most cases to the genus by using hair characteristics. Hairs were studied by direct examination in balsam for medullary and pigment characters, and by plastic impressions for studying cuticular scales and for making measurements.

In almost all bats the cuticular scales are coronal in form, and the conventional terminology for describing these scales was found to be inadequate. Established terms in use by botanists for describing coronal leaf forms were adopted, so that words such as "appressed," "divaricate," "dentate," "hastate," "repand," "crenate," "erose," and "lobate" now appear as mammalian morphological terms. Relatively few bats have hair showing a medulla, but often there is pigment not associated with medullary structures.

In general, the relationships established by the study of hair structure bear out currently recognized taxonomic relationships, but in some areas it suggests a need for restudy, and in many cases it supports the current trend toward a reduction in the number of genera. Hair structure is more diversified in the Megachiroptera than in the Microchiroptera; however, in the latter each family has a predominant structural pattern, whose variations as a rule allow generic identification.

A brief introductory section contains the discussion of the subordinal and familial characteristics and the key, and takes up only 41 pages. The remainder of the volume is devoted to a tabular presentation of the data. For each genus the characteristics of the scales, medulla, pigment, and filament structure are tabulated, along with a statement of the genus' geographic distribution, accepted taxonomic position, and affinities as indicated by its hair structure. At the end are 9 plates illustrating the variety in structure that may be found in hairs from bats of various kinds.

BRYAN P. GLASS

ECONOMIC ZOOLOGY

ON THE DYNAMICS OF EXPLOITED FISH POPULATIONS. *Ser. II, Vol. XIX.*

By R. J. H. Beverton and S. J. Holt. Her Majesty's Stationery Office, London. £6 6s. 533 pp.; ill. 1957.

Two of the most important and widely recognized goals of fishery science are the rational exploitation and prognostication of fish populations. This work, a sophisticated synthesis of biology and mathematics and a monument to its authors, is a highly successful leap toward a new status, one with the basic tools for achieving these ends. Traditionally, fishery research and management have been carried out piecemeal, more or less, throughout the world. Until now, few attempts have been made to integrate, evaluate, and develop this material critically into a broad, realistic body of working principles. The authors have consummated these long-range objectives after eight years of effort from first-hand field work and by utilizing the fruits of other scientific investigators on the vital statistics of the North Sea plaice, haddock, cod, sea herring, yellow perch, and many others of inland waters. They boldly claim, and with some justification, that, given the right data, they can solve any problem in fishery regulation today. Without doubt they have reached a point where, by their approach, they can scientifically dissect many regulatory crises in the fishing industry, but since these are so inextricably interwoven with socioeconomic and political factors, such a boast should be reexamined.

Beverton and Holt, both British zoologists with strong mathematical backgrounds and extensive experience at sea, propose precise methods of attacking the problem of the best use of fish stocks under the stress of fishing. Always cognizant of the biological implications of their work, they do this by setting up mathematical models to represent the interaction of the factors that govern the annual yield of a fishery and the abundance of a fish stock, on which depends the well-known index of relative abundance called the catch-per-unit-of-fishing-effort. These models were successfully tested, using empirical data derived from the North Sea fisheries and from the worldwide literature on the subject. Incidentally, this feature represents very great progress, since Volterra, Lotka, Kostitzin, Gause, and more recent pioneer model-builders in the study of animal populations were generally unable to test the basic assumptions of their respective theories.

The four primary processes in fish populations hunted by man have been formulated in quantitative detail: (1) recruitment from reproduction or movements; (2) growth in length and weight; (3) fishing mortality; and (4) natural mortality. These are brought together by considering a year-class (or cohort of fish born during any one year) of recruits to the fished area and applying the other three factors represented in the appropriate mathematical forms, to deduce what the total yield from the year-class would be throughout its life in the fishery. Ultimately, the authors investigate, by elaborating the simple model, the effects of changing each of the primary factors and keeping the others constant, prior to studying the effect of changing all together. Their ideas and techniques are developed with a neatness and clearness that is truly a wonder to behold.

The book is divided into four parts: (1) fundamentals of the theory of fishing, illustrated by analysis of trawl fishery; (2) some extensions of the simple theory of fishing; (3) estimation of parameters; and (4) the use of theoretical models in a study of the dynamics and exploitation of fish populations. Readers will find that the first two parts are theoretical, while the fourth part deals the most with practical applications. Beverton and Holt develop equations and illustrate fitting methods with unusual clarity for many and diverse topics in fishery science. Some of these are: recruitment in relation to stock density; variation in the natural mortality rate with age; variation in growth rate; effects of predation by fish on the biomass and yield; use of recaptures from marking experiments; selectivity of various sizes of mesh in nets; principles and methods of fishery regulations.

Many readers will be interested in the excellent description of the theory and background of mathematical model-building, which utilizes basic algebra, differential calculus, and conventional biostatistical methods. The authors, in an interesting departure from the advanced treatment of population dynamics, avoid stochastic models, in which probability theory is used to determine their functional relationships. An exception is in their development of egg-recruit relationships, although certainly other biological phenomena behave in a stochastic manner. They subscribe to and largely utilize "old-fashioned" deterministic models, in which the factors responsible for the changes of a population are assigned constant numerical values. Although fishery biologists are beginning to recognize that populations do not fluctuate deterministically, the authors believe that the derivation of stochastic equations is so burdened with great labor, low standard of accuracy in the data, and biological variables of great complexity, that their "simple" and conservative approach is the most practical. This decision will result in a mixed reception of their models.

Although this book will have an immediate appeal to the minority of mathematically trained zoologists and ecologists, other biologists who are usually intimidated by too much mathematics in their professional literature can use it with great profit. It would be well for the average worker to begin with the plainly-written Résumé at the end. Perhaps a logical second step, rather than turning to the text, would be to read the elementary paper entitled, "Some simple mathematical models as aids in interpreting the effect of fishing," (K. D. Carlander, *Iowa State Coll. J. Sci.* 32: 395–418. 1958). Then one can graduate to the shorter and somewhat more palatable contribution by Beverton and Holt in the book, *Sea Fisheries; Their Investigations in the United Kingdom* (edited by M. Graham, E. Arnold, London, pp. 372–441. 1956). Finally this text should be attacked, preferably late at night when all is still. If one can run this gauntlet, the rewards will be great in terms of new perspective.

In spite of the elaborate treatment given the subject—a part of which incidentally could have been expressed much more simply—this amazing book can contribute to progress in many very diverse disciplines concerned with biological populations. As far as fishery science itself is concerned, the authors never lose sight of the enormous hurdles to be made before the field is on a strong and predictable basis. Humility is evident as they endorse the time-honored adage that "... the best management of fishing is to leave it alone until events show that intervention is necessary." Their enthusiasm and accomplishment, however, are better expressed by a quotation by Graham, who reminded the delegates at a U. N. marine resources conference about ten years ago that "... life does not stand still while specialists put their minds in order." Everything about the book, save its price, is inspiring and stimulating. Every library or investigator concerned with populations should have access to it, for few published works can open up so many new vistas as this one.

ROMEO MANSUETI

THE EFFECTS OF ATOMIC RADIATION ON OCEANOGRAPHY AND FISHERIES. *Report of the Committee on Effects of Atomic Radiation on Oceanography and Fisheries of the National Academy of Sciences Study of the Biological Effects of Atomic Radiation. Pub.* 551.

National Academy of Sciences—National Research Council, Washington, D. C. $2.00. x + 137 pp.; ill. 1957.

One of the ironies of fishery research is that it is illegal from a public health viewpoint for experimentalists to use radioisotopes in the field on marine organisms that are potentially a source of human seafood, and yet uncontrolled nuclear explosions continue and some controlled radioactive wastes have produced large-scale contamination problems among fishes and shellfish in their aquatic environment. Two highly publicized cases in point are: (1) the international incident between the United States and Japan over radioactive tuna harvested during and after atomic detonations at Bikini; and (2) the astonishing ability of Pacific Ocean clams and other organisms in nature to accumulate radioactive cobalt-60 from water containing trace amounts, an unexpected phenomenon in the tests. In view of the progressively important aspects of radioecology, few topics at this time are so vital to all of us.

As with many new crucial stages in the progress

of civilization, ignorance and emotionalism have characterized much of the discussion of radioactivity and the fisheries. This book attempts to correct, to a high degree, many of those misconceptions and provides the proper background for future thinking and design. The most ominous message conveyed is the following: within the foreseeable future the problem of industrial atomic waste disposal will greatly overshadow the present problems posed by the dispersal of radioactive materials from bomb tests. Since the ecological aspects of waste disposal can present serious limiting factors to the full exploitation of atomic energy in the future, solutions must be fully explored today. Another serious conclusion: although it may be convenient or perhaps necessary to dispose of such industrial wastes in the oceans, at present it is not possible to predict the effects of such disposal on man's use of fishery resources in the sea. The current situation is that in the storage and disposal of dangerous high-level wastes in tanks, scientists of the Atomic Energy Commission have reached a very critical stage. This book suggests that the radio-ecologist will be called upon more and more to help provide a solution. Low-level liquid wastes, while usually not stored in containers, are discharged in enormous quantities into large rivers, the sea, and the soil; hence they also are and will be of increasing concern to aquatic biologists.

This volume culminates three meetings held in the spring, 1956, of this special committee dealing with the specialized aspects of the biological features of atomic radiation. Financed by a grant from the Rockefeller Foundation, the work consists of an introduction and 13 chapters by a total of 20 people, all of whom are top experts in the field of hydrobiology and nuclear physics. The introductory section represents an excellent and general summary of oceanography and the ecology of marine organisms. In a sense, too, it is a hasty reconnaissance of the entire book. Moreover, it is the most up-to-date synthesis of information on radioactivity and its pertinence to the disposal of "hot" wastes in the ocean. The contributions cover in detail the use of tracer techniques, used both for the measurement of physical and chemical processes in the sea and atmosphere, and for large-scale biological experiments.

The results of laboratory experiments on the uptake and the accumulation and loss of radionuclides by marine organisms in the three trophic levels suggest the complexity of this topic. At the first level, for example, different species of planktonic algae, as exemplified by *Nitzschia*, had remarkably different abilities to concentrate a particular element from the sea water medium. The crustaceans and mollusks, at the second level, accumulated strontium rapidly from sea water, and when radioactive shellfish were returned to a normal sea water environment, the radioactivity present in the tissues declined rapidly to about one-tenth of the maximum concentration. Fast-swimming pelagic fishes, such as tunas and menhaden, and the bottom-dwelling croakers, at the third level, excreted strontium rapidly from soft, visceral tissues, but, as is well known, the bony structures, gills, integument, and muscles retained it for a long period. Obviously, the results of these few experiments are so tentative that they can be extrapolated only with extreme caution. They emphasize the point, nevertheless, that although oceanic disposal seems practical because of the sea's large dilution factor, the tendency of the large standing crops of shellfish and other marine organisms in shallow coastal areas and estuaries to concentrate isotopes, and thus present great economic problems in the seafood industry, may overshadow this advantage.

The conclusions and recommendations, while broad and urgent, highlight the important fact that an adequate and long-range program on all aspects of oceanic research must be set up immediately, if we are to avert serious military, political, and economic crises in the future. Although the problems of radioactivity in the natural environment are not yet overwhelming, they soon may be. The book is a plea for the current and intensive probing into all facets before serious contamination in our waters occurs. It will serve as a catalyst in this direction for a long time to come. For this reason, a glossary, cutting through all the disciplines that contributed to the report, plus an index, would have enhanced its usefulness considerably. The symposium, nevertheless, will be an authoritative reference work for a wide variety of biologists and persons in adjacent fields for some time to come. The fact that the book is a rare bargain in these times of high printing costs lends substance to this point.

ROMEO MANSUETI

THE INTRODUCED REINDEER OF SOUTH GEORGIA. *Falkland Islands Dependencies Survey; Scientific Reports, No. 22.*

By W. Niger Bonner. Her Majesty's Stationery Office, London. 7s. (paper). 8 pp. + 3 pl.; text ill. 1958.

THE UFAW HANDBOOK ON THE CARE AND MANAGEMENT OF LABORATORY ANIMALS. *Second Edition (greatly enlarged).*

Edited by Alastair N. Worden and W. Lane-Petter; foreword by Sir Harold Himsworth. UFAW (The Universities Federation for Animal

Welfare), London. 70s. xx + 951 pp.; ill. 1957.

Our debt to laboratory animals, for the advances in medical and allied sciences which their use has made possible, obliges us to see that the conditions in which they are housed and the way in which they are maintained should be the most humane that can reasonably be provided. Another very good reason for giving laboratory animals the best possible care is that only well-managed stock can provide living material of the quality which medical research demands; and in fact, inferior animals may lead and very often have led to confusing, or even useless, results. Thus, from both the humanitarian and technical points of view, there is an overwhelming case for providing laboratory animals with the best care and conditions that are reasonably practicable before and during experimental work; and these two interests, far from being in conflict, are synergic.

In the present volume the chapters are grouped under various main headings. Part 1, comprising the first 16 chapters, deals with general considerations common to all or nearly all laboratory animal problems. In so far as the subject matter of this part is common to a number of species, it is dealt with in a general way, and in the main is excluded from the chapters on individual species. The handbook naturally presents British experience, and thus describes a number of practices that differ from the American. Therefore, persons considering the initiation of research on various rodents, birds, reptiles, fish, or even insects or earthworms should consult this manual. For each species valuable detailed information is collected about breeding, feeding, caging, and transporting the animals.

D. E. Davis

Advances in Pest Control Research. *Volume 1. Edited by R. L. Metcalf. Interscience Publishers, New York and London.* $11.00. vii + 514 pp.; ill. 1957.

This series is to be devoted to recent significant research on all phases of pest control, pests being defined as plants and animals that compete with man for food, attack his person, or damage his possessions. The emphasis is to be on the fundamental aspects. This first volume certainly meets the standards set forth in the Preface by the editor, R. L. Metcalf of the University of California, Riverside.

The control of health hazards associated with the use of pesticides is discussed objectively by J. M. Barnes of the Medical Research Laboratory, Surrey, England. This is an excellent summary for those biologists unfamiliar with the use of pesticides. A. S. Crafts of California discusses the chemistry and mode of action of herbicides; T. R. Fukuto of California, the organo-phosphorus insecticides; and J. G. Horsfall of Connecticut, mechanisms of fungitoxicity. W. E. Ripper of Cambridge, England, reviews developments in the use of systemic insecticides. G. F. Shambaugh, R. F. Brown, and J. J. Pratt, Jr., of the Army Quartermaster Research and Engineering Center, Natick, Massachusetts, have summarized work on repellents, including a section on chemical structure and repellency. Control of soil fungi is discussed by J. B. Kendrick, Jr., and G. A. Zentmeyer of California.

There are three articles on methods. Paul A. Dahm of Iowa writes on the use of radioisotopes in pesticide research; M. S. Shecter and I. Hornstein of the Agricultural Research Service, Beltsville, Maryland, on chemical analysis of residues; and Y. P. Sun of Denver, Colorado, on the bioassay of residues.

Researchers in this field will find this volume of great value. It fills the purpose of providing authoritative summaries of recent developments in a very important field in which a large number of chemists, entomologists, plant pathologists, and plant physiologists are working.

Neely Turner

ANIMAL GROWTH AND DEVELOPMENT

Foundations of Embryology. *By Bradley M. Patten. McGraw-Hill Book Company, New York, Toronto, and London.* $10.50. xvi + 578 pp.; ill. 1958.

The author of *Embryology of the Pig, Human Embryology,* and *Early Embryology of the Chick* has in this book attempted to assemble a text equally suitable for the non-science major, the premedical student, and the student preparing for a career in biology. The verb "assemble" is chosen with good reason, for of the 539 pages (including illustrations) of text, some 46 pages are newly composed for this book, while some 13½ pages have been rewritten. The remaining 479-odd pages are taken directly, with changes only of a word or two here and there, from the three previous texts of the author cited above. Similarly, of the 313 figures, some 291 are reproduced from these earlier books, 7 illustrations are redrawn, and 15 are new or from other sources.

The construction of a "new" text from three old ones poses problems of continuity, of the avoidance of repetition, and of updating, none of which has been entirely met. The transitions back and forth from one precursor book to another are in places abrupt, while in other places they have been smoothed over by "bridge passages." At first reading it seems strange to find the Latin origin of "morula" given both on p. 84 and on p. 87. It becomes more comprehensible when one perceives

that the paragraphs in question are from *The Chick* and *The Pig* respectively.

A lack of comprehensive updating, however, is the most serious flaw. And if a thorough understanding of the early phases of embryonic development is regarded, as I do personally, as being of primary importance for the beginning student, it is just here that this text is least reliable. In the section dealing with meiosis, for instance, (a section which, incidentally, has been rewritten), we are treated to the lengthwise "splitting" of chromosomes; we are told on p. 45 that "the chromosomes take shape from the scattered chromatin granules of the resting nucleus," and on p. 48 that "during prophase the spireme thread was broken up into chromosomes." The rest of the discussion of meiosis continues similarly. A preceding discussion of the vicissitudes of the germ plasm, its quality and transmissible defects in it, seems equally anachronistic.

A proper comparison of pregastrular stages among the chordate classes is prevented by the assignation of homologous status to cavities rather than to the tissues out of which, after all, an embryo is built. Thus the subblastodermal space of bird embryos and the blastocyst cavity of mammalian embryos are both considered to represent the blastocoel, which thereby becomes extra-embryonic. The figures illustrating amphibian gastrulation perpetuate a venerable error concerning the origin of the dorsal mesoderm and endoderm. In fact, Vogt's accurate illustrations are modified to include this fallacy. The thickness of the neural plate, as well as its folding to form a tube, is attributed to cell proliferation. A figure indicates the wall of the early neural tube as a syncytium, although the text adds a possible qualification to this. Cephalic precocity is explained as a manifestation of the law of recapitulation, to which tribute is paid elsewhere as well. Further confusion comes about by the use of the term "growth" to include a variety of morphogenetic movements. Such examples suffice to indicate the general weakness of this book in areas pertaining to early development and preparation for it.

Once the basic body plan is arrived at, the author finds himself in more congenial surroundings, and from this point onward with few exceptions, vertebrate development as exemplified by bird and mammal embryos is lucidly, and to the best of my knowledge, accurately described, as well as clearly illustrated. The development of the circulatory system in particular is most superbly presented, together with recent material on the subject, as one would expect in view of Patten's long personal connection with studies in that area. It is unfortunate, however, that the excellent drawings of representative cross sections of a 9.4 mm pig embryo are distributed throughout the text rather than assembled in one place, where they would more usefully serve an an adjunct to laboratory study.

It should be noted that fairly little is done to introduce the reader to the experimental basis of our embryological knowledge. If embryology is to capture the interest and liberate the creative imagination of young minds, it will most readily be accomplished through allowing the developing intellect to share vicariously in the thrill of discovery.

While the author has not succeeded in constructing a superior textbook for either general or specialized zoology students, the book may find favor for use in the instruction of students whose primary concern is to be with the later stages of development.

MALCOLM S. STEINBERG

THE EMPEROR PENGUIN, *Aptenodytes forsteri Gray. II. Embryology. Falkland Islands Dependencies Survey; Scientific Reports, No. 10.*

By T. W. Glenister. Her Majesty's Stationery Office, London. 17s. (paper). 19 pp. + 8 pl.; text ill. 1954.

A NEW METHOD OF AGE DETERMINATION IN MAMMALS WITH SPECIAL REFERENCE TO THE ELEPHANT SEAL (*Mirounga leonina* LINN.). *Falkland Islands Dependencies Survey; Scientific Reports, No. 2.*

By R. M. Laws. Her Majesty's Stationery Office, London. 3s. (paper). 11 pp. + 1 pl.; text ill. 1953.

THE ELEPHANT SEAL (*Mirounga leonia* Linn.). *I. Growth and Age. Falkland Islands Dependencies Survey; Scientific Reports No. 8.*

By R. M. Laws. Her Majesty's Stationary Office, London. 20s. (paper). 62 pp. + 5 pl.; text ill. 1953.

ANIMAL MORPHOLOGY

ANATOMY OF THE CHORDATES. *Second Edition.*

By Charles K. Weichert. McGraw-Hill Book Company, New York, Toronto, and London. $9.50. vii + 899 pp.; ill. 1958.

Weichert has devoted a full measure of time and energy to an extensive revision of his well-received text. The new edition is some 22 pages shorter than the first, but it is still a weighty volume aimed at the two-semester course in comparative anatomy. The reduction in total pages is a little surprising, for all but two chapters have been expanded.

Chapter Two, on the classification and evolution of the chordates, an introduction to the scope of the chordate group, has been drastically reduced and many figures eliminated. This is where most of the pages have been saved. The author has rewritten a good portion of the text, mindful of the criticisms of the first volume. He has eliminated the embassassing errors that slipped in, and has added new information either in an attempt to clarify a concept or to bring functional aspects up to date. A number of old figures have been removed, some redrawn, and a good group of new ones added. The most noticeable additions are those related to embryology. Unfortunately, this is a chapter that makes the least difference to the anatomist.

The general organization of the text has not been changed. It is still reasonably divided into three parts. Part One (3 chapters) reviews the Phylum Chordata. Part Two (11 chapters) treats the comparative anatomy of organ systems. Part Three (4 chapters) is essentially a laboratory manual for the lamprey eel, spiny dogfish, necturus, and cat. The three parts are followed by one summary chapter that is essentially classification.

It should be noted that Part Three has been reworked carefully to make it more easily used by the student. The material has been reorganized, but, most important, the key words have been set in bold-faced type so that the eye will catch them. The book can more readily be used while dissection is in progress.

A major weakness of this text is its complete lack of bibliographic guidance for either student or professor. Not even the major textual references are mentioned; where controversial interpretations are presented, there is no way to discover who influenced Weichert's thinking.

The volume is well-balanced in presentation and does not overdo the author's particular interest. It is not even apparent which system is most to the author's own liking. The text is a worthy contribution, better than the first edition, and ought to find ready acceptance by both students and teachers of comparative anatomy.

IRA B. HANSEN

STUDIES ON THE STRUCTURE AND DEVELOPMENT OF VERTEBRATES. *Volume 1, Chapters 1–8; Volume 2, Chapters 9–14.*

By Edwin S. Goodrich. Dover Publications, New York; Constable & Company, London. $2.50 per vol. (paper). (1) lxx + 485 pp.; ill. (2) iii + pp. 486–837; ill. 1958.

These two fine paperback volumes are reprints of the one-volume 1930 edition, to which an obituary of E. S. Goodrich has now been added. The printing, binding, and illustrations are of good quality typical of the publisher; as usual, they have chosen wisely among the older scientific books. One small request, however, might be addressed to the publisher: that all clues to the original date of the book being reprinted without revision *not* be so painstakingly avoided, both in the volume and advertising brochures. The date of writing is an important piece of information, and one should not have to approximate it by inference from text and bibliography.

DAVID R. EVANS

FUNCTIONAL NEURO-ANATOMY, *including an Atlas of the Brain Stem. Third Edition.*

By A. R. Buchanan. Lea & Febiger, Philadelphia. $7.50. 362 pp.; ill. 1957.

The third edition of this text is only slightly changed from the previous edition (*Q.R.B.*, 27: 324. 1956), except for the expansion of a few sections, particularly the description of the extrapyramidal motor system. Although not outstanding, this book presents a concise introduction to the subject, which is, for the most part, clear and easy to read.

Certain areas in neuroanatomy are difficult to present, and deserve special notice. Cerebellar pathways are well described, but the correlation of function with neuronal circuits is confusing. The components and connections of the extra-pyramidal system are shown in some detail, but may not give the student an integrated understanding of this difficult area. The chapter on the hypothalamus mentions many of the recent findings, but in a rather piecemeal fashion. The arterial supply of the brain, although quite accurately described in the text, is not illustrated in sufficient detail. Finally, the atlas of serial sections is clearly labelled, but the photographs are too small for comfortable study.

NEAL NATHANSON

HEMATOLOGY *for the Medical Technologist. Second Edition, Revised.*

By Charles E. Seiverd. Lea & Febiger, Philadelphia. $5.75. 275 pp. + 13 pl.; text ill. 1958.

This is a compact and clearly written manual containing most of the information useful as an introduction to hematology for the medical technologist and the various techniques used in a general hematology laboratory. There are many excellent plates and diagrams illustrating materials and methods. Those showing red and white blood cell morphology, however, are small and the color somewhat atypical, defects which limit their value. The techniques of the various procedures are described clearly and concisely. The medical information associated with the various tests is occasionally not

too accurate, such as to detract somewhat from the value of the book; but this is not a major disadvantage, since the book is not designed for medical students or physicians. The section on blood grouping employs the terms "agglutinogens" and "agglutinins," which may be unnecessarily confusing to beginners.

Since inaccurate blood counts may be worse than none at all, one cannot agree with the recommendation for one-chamber red and white cell counts. Estimation of platelets on smear, microhematocrits, Dacie's osmotic fragility method, and the washing of counting chambers (rather than wiping) are other omissions which could be remedied for the sake of completeness. This small volume can be recommended for medical technicians who are just beginning training, as a step-wise guide to common hematological procedures.

LOUIS K. DIAMOND

A REVISED INTERPRETATION OF THE EXTERNAL REPRODUCTIVE ORGANS OF MALE INSECTS. *Smithsonian misc. Coll., Vol. 135, No. 6, Pub. 4309.*

By R. E. Snodgrass. Smithsonian Institution, Washington. Free upon request (paper). iii + 60 pp.; ill. 1957.

THE GENERAL HISTOLOGY AND TOPOGRAPHIC MICROANATOMY OF *Australorbis glabratus*. *Bull. Mus. comp. Zool., Harv., Vol. 119, No. 3.*

By Chia-Tung Pan. Museum of Comparative Zoology, Cambridge. $1.60. (paper). ii + pp. 237–299 + 18 pl. 1958.

NATAL PLUMAGES AND DOWNY PTERYLOSES OF PASSERINE BIRDS OF NORTH AMERICA. *Bull. Amer. Mus. nat. Hist., Vol. 113, Art. 5.*

By David Kenneth Wetherbee. American Museum of Natural History, New York. $2.00 (paper). iv + pp. 343–436; ill. 1957.

ÉTUDE D'UN TYPE D'OISEAU-AFRICAIN: *Corvus albus. Généralités—Ostéologie. Inst. franç. Afr. noire, No. XVI.*

By P.-L. Dekeyser and J. Derivot. Institut Français d'Afrique Noire, Ifan-Dakar. 540 fr. (paper). *58 pp.; ill. 1958.*

DENTAL PATTERNS IN MICE of the Genus *Peromyscus*. *Misc. Publ. Mus. Zool. Univ. Mich., No. 99.*

By Emmet T. Hooper. Museum of Zoology, University of Michigan, Ann Arbor. 75 cents (paper). 59 pp.; ill. 1957.

ANIMAL PHYSIOLOGY

ANATOMIES OF PAIN.

By K. D. Keele. Charles C Thomas, Springfield, Ill. $5.50. x + 206 pp. + 13 pl.; text ill. 1957.

The author proposes to trace the growth of anatomical and physiological concepts of pain "which lie, often unconsciously, at the roots of our present ideas." He succeeds in this task. After he has skilfully traced the history of pain concepts from the earliest time to the present, many of the answers which we give to the problem of pain begin to sound like restatements of similar answers given by the ancient Egyptians, Indians, Greeks, and Romans. Leriche's present-day theory of pain localization, for example, does not seem essentially different from Democritus' and Lucretius' postulate that pain is localized in the body part stimulated. Also, the Aristotelian idea of a sensory center correlating all sensory impressions—the *sensorium commune* or "seat of the soul"—is still with us. The reticular system in the brainstem, which at the present time is receiving the accolades of the *sensorium commune*, is only the latest of a series of anatomical parts—heart, anterior ventricle, pineal gland, stomach, cerebrum, medulla—which have held this title at one time or another.

A history of research on the physiology and anatomy of pain includes, of necessity, a history of nerve physiology in general. After reviewing the work which led to the Bell–Magendie law and to Müller's theory of specific nerve energies, the author traces the investigations which resulted in the conception of specific functions for the various tracts in the spinal cord, and gives special emphasis to the conception of the pain pathway as localized in the anterolateral tract. He then reviews the more recent investigations which suggest the revolutionary conclusion that pain transmission cannot be localized in specific neuronal paths in the cord and that the anatomy of "the pain pathway" can be best viewed as "one of statistical probability."

The latter portion of the book, which reviews work during this century, is a concise summary of our present knowledge of the physiology and psychology of pain. All psychologists, biologists, and clinicians concerned with sensory-perceptual processes will find this monograph valuable.

THEODORE X. BARBER

MUSCLE RELAXANTS IN ANESTHIOLOGY. *American Lecture Series, Publication No. 294.*

By Francis F. Foldes; illustrated by Margaret M. Croup. Charles C Thomas, Springfield, Ill. $5.50. xx + 210 pp.; ill. 1957.

One welcomes the appearance of this concise volume on the skeletal muscle relaxants. The author's broad experience as an experimental pharmacologist and clinical anesthesiologist is reflected in this book.

The scope of the book extends from the history of muscle relaxants, their chemical constitution, and the physiology of neuromuscular block to the clinical application of these agents in the field of anesthesiology. The relationship of muscle relaxants in other areas of clinical medicine is also discussed. Special reference is made to the use of muscle relaxants in electroshock therapy in the treatment of mental illness.

The author's coverage of the field is comprehensive, including details of dosage schedules for individual muscle relaxants. A discussion of antidotal measures in cases of overdosage is also included. The illustrations of the supposed sequence of events at the myoneural junction, showing the blockade of acetylcholine by the various types of muscle relaxants, are excellent. The author exhibits a felicity of diction which is commendable. This book is recommended enthusiastically to all those interested in pharmacology and anesthesiology.

JOHN C. KRANTZ, JR.

NEUROLOGIC EXAMINATION OF THE DOG *with Clinicopathologic Observations.*

By John T. McGrath. Lea & Febiger, Philadelphia. $5.00. 181 pp.; ill. 1956.

This book is designed for the veterinary practitioner as an introduction to neurologic diseases of the dog. The early chapters discuss the clinical history, physical examination, and pertinent laboratory tests, and roughly follow the methods of clinical medicine. Reference is made to the extensive experimental literature, which is integrated to provide a rational approach to the analysis of symptoms. The later chapters review those neurologic diseases which commonly occur in the dog, with extensive documentation from the author's clinical experience, and will provide a very useful orienting background. In summary, this book presents an orderly introduction to the subject and should lead to a more rational and thorough approach to this difficult aspect of veterinary practice.

NEAL NATHANSON

TRANQUILIZING DRUGS. *A symposium of the American Association for the Advancement of Science.*

Edited by Harold E. Himwich. American Association for the Advancement of Science, Washington. $5.00; (AAAS Members, $4.50). viii + 197 pp.; ill. 1957.

The symposium of which this volume is a reprint was held in 1955. Since research concerning tranquilizing drugs is a relatively new and very popular field, these reports are becoming out of date in the passage of nearly four years and probably do not reflect current status of the subject. Thirty contributors presented 14 papers under the following headings: Electrophysiological Analysis, Metabolic Analysis, and Therapeutic Considerations.

APPLIED PHYSIOLOGY OF THE EYE.

By H. Willoughby Lyle; assisted by T. Keith Lyle. Ballière, Tindall & Cox, London; [*Williams & Wilkins Company, Baltimore*]. $9.00. viii + 341 pp.; ill. 1958.

The title of this textbook is somewhat unfortunate, since it means different things to different people. The sense used here is "as applied to medicine," which is a usage more common in England than in the United States.

In the Preface the author states that it is "his endeavor to help those who are working for higher examinations in Ophthalmology such as F. R. C. S. in Ophthalmology, the Mastership of Surgery in Ophthalmology, and the diploma of Ophthalmology." It is evident, therefore, that the author is thinking in terms of practicing ophthalmologists and the multitude of clinical miscellanea that they are expected to know in order to pass examinations. The organization of the material is somewhat confused. Approximately two-thirds of the text adheres to the convention of beginning with the eyelids, and in successive chapters treating structures in an anatomical progression to the optic nerve. The remaining chapters discuss subjects (like diabetes mellitus, vitamins in ophthalmology, ocular tension, etc.) which the author feels necessary to include but which do not fit easily into any scheme, and which therefore lack obvious continuity.

There is heavy stress on the anatomical relationships of the various structures. Functional relationships, however, are treated sparingly or not at all.

A typical chapter begins with a discussion of the anatomy of some part of the eye. This is followed by a brief mention of the normal physiology. More considered attention is then devoted to pathological conditions involving the structure. Unfortunately, physiology is generally treated in a superficial and casual manner, even in important areas where much is known. This is particularly illustrated in the chapter on ocular tension and in the section on the pathological entity of retro-lental fibroplasia. Both of these have recently been very thoroughly studied and offer unusual opportunities for a discussion of the pathogenic disturbances.

Exactly 32 illustrations were counted; these were

line sketches of anatomical relationships—presumably made by one of the authors. Although the amount of illustrative material is sparse, the sketches are clear and informative.

This text is so sharply directed toward the student preparing for higher examinations in clinical ophthalmology, as pointed out by the author, that it has limited usefulness otherwise.

H. G. WAGNER

PHOTORECEPTION. *Ann. N. Y. Acad. Sci., Vol. 74, Art. 2.*

By Jerome J. Wolken and 32 contributors. The New York Academy of Sciences, New York. $3.50 (paper). ii + pp. 163–406; ill. 1958.

ELECTROPHYSIOLOGY OF THE VISUAL SYSTEM. *Symposium held at Wilson Hall, National Institutes of Health, Bethesda, Md. Amer. J. Ophthal., Vol. 46, Ser. 3, No. 3, Pt. 2.*

Edited by M. G. F. Fuortes; 35 contributors. Ophthalmic Publishing Company, Chicago. Free upon request from M. G. F. Fuortes, N. I. M. D. B., N. I. H., Bethesda 14, Md.; (paper). 182 pp.; ill. 1958.

The conferences upon which these books are based were held less than a month apart at the beginning of 1958. Both editors are to be congratulated on the speed with which they have been able to get their respective volumes into print. The two books have similar purposes and contents, and in a few places the contents are even identical.

The papers in *Photoreception* are somewhat arbitrarily divided into 3 sections. The first section, on Photoreceptor Structures, includes papers on the fine structures of various invertebrate and vertebrate photoreceptors (Wolken, Miller), histochemical examinations of the retina (Sidman), the optics of the insect eye (de Vries and Kuiper), and the integration of receptor activities as related to neural interaction in the eye (Ratliff, Miller, and Hartline).

The section on the Biochemistry of Photoreceptors has papers on the visual pigments and electroretinogram of the bee (Goldsmith), the natural history of the visual pigments (Crescitelli), and the nutritional causes of nightblindness (Dowling and Wald). The visual pigments and their bleaching are examined in several papers: the kinetics of human cone pigments in vivo (Rushton); the mechanism in vitro of bleaching rhodopsin (Wulff et al.); the flash photolysis of rhodopsin in solution (Kropf and Hubbard); models of the photochemical part of the visual process (Oster); and energy transfer in ordered and unordered systems, especially in chlorophyll (Tollin et al.).

The physiology of photoreception, the last section of *Photoreception*, includes papers on the caudal photoreceptor of the crayfish (Kennedy), on visual cell viability and differentiation in mammals (Noell), on centrifugal influence on the electroretinogram in mammals (Jacobson and Gestring), and on human retinal responses (Riggs). There are also papers on the sensitivity of the human eye (Pirenne), retinal mechanisms for chromatic and achromatic vision in the fish (Svaetichin and MacNichol), and an analysis of the receptive fields of ganglion cells in the cat retina (Wiesel and Brown). The illustrations in this section are very good reproductions of the originals, especially the light and electron micrographs. Much of the material in this symposium has not been published elsewhere.

This volume is not a completely accurate record of the conference that it is based upon; two of the lectures actually given are not represented by papers, and none of the generally spirited and occasionally caustic discussions have been included. This remark does not imply that the book is not very good, for it is that, but merely expresses the wish that the book were perfect.

Electrophysiology of the Visual System includes a dozen papers covering most of the major lines of research in the visual system. There are reports on the responses to electrical stimulation of the *Limulus* eye (Lipetz); on the crayfish caudal photoreceptor (Kennedy); the characteristics of color receptors in the fish retina (MacNichol and Svaetichin); visual fields of single units in the frog (Wagner and Wolbarsht); electrical responses from the toad eye (Gouras), and the cat eye (Brown and Wiesel); and a comparison of responses from the eye and optic tectum of the chicken (Crampton). The physical factors modifying the human electroretinogram as a function of wavelength (Dodt), temporal periodicities in the primary visual projection system of the cat (Marshall), and cortical unit responses in unanesthetized cats (Hubel) are also described. Two papers with marked clinical references are included: the electromyograms of human extraocular muscles (Breinin), and the electroretinograms of humans suffering from various retinal pathologies (Goodman and Gunkel).

Most of these papers are original reports and will not be duplicated in other literature. An almost stenographic transcript of the discussions following each of the papers is given, and much of the value of the book is here. Many of the participants "just happened to have a few slides" with them, and very interesting slides they were in most cases. The discussions contain reports on the electrical response to a single quantum of light in the *Limulus* eye (Yeandle), on the electroretinograms of several species of lizards and turtles (Forbes), and on the effects of vitamin-A deficiency on the rat electroretinogram (Dowling and Wald). In addition, much other miscellaneous information is included which per-

tains to electrophysiological research in general, such as types of electrodes and electrode-tip-locating methods.

Since the discussions do not always refer to the papers that preceded them, some rearrangement by the editor might have made the book a more logical whole. However, given the choice between a record of the discussion as it occurred, or none at all, the record on whatever terms it is presented is preferable. Some comments are more valuable than the paper they concern.

Both *Photoreception* and *Electrophysiology of the Visual System* are books that everyone interested in sensory physiology from a comparative viewpoint, whether as a researcher or a teacher, should have available for ready reference. It is to be hoped that the records of future conferences on visual physiology will maintain the high standards established in these two.

MYRON L. WOLBARSHT

THE ELEPHANT SEAL (*Mirounga leonina* LINN.). III. *The Physiology and Reproduction. Falkland Islands Dependencies Survey; Scientific Reports No. 15.*

By R. M. Laws. Her Majesty's Stationery Office, London. 27s. 6d. (paper). ii + 66 pp. + 5 pl.; text ill. 1956.

ANIMAL NUTRITION

BIBLIOGRAPHY OF FOOD. *A Select International Bibliography of Nutrition, Food and Beverage Technology and Distribution, 1936–56.*

By E. Alan Baker and D. J. Foskett. Academic Press, New York; Butterworths Scientific Publications, London. $11.00. xii + 331 pp. 1958.

The *Bibliography of Food* covers books, journals, pamphlets, government publications on nutrition, food economics, and food technology. It includes material published between 1936 and 1956, although a few publications prior to 1936 are also included. The bibliography does not cover articles published in periodicals, although the journals themselves are listed together with the addresses of the publishers and some comment as to the type and quality of articles published by each particular journal.

The subject is broken down into two categories: first, from an operational viewpoint, into topics such as distribution, marketing and retailing, food control and rationing, food manufacture, food preservation; second, on the basis of commodities, such as milk, milk products, sugar, tea and coffee, bakery, and edible oils. In most cases a general statement regarding the contents of the publications is given. The authors have, in many cases, characterized the subject matter so that the reader can determine whether a publication is primarily practical or theoretical. Publications relating to cookery, catering, and home use have generally been excluded.

The authors have been most thorough with respect to the bibliography. The table of contents is complete and well organized. The index, by both subject and author, is also most helpful.

This book ought to be very useful to any organization concerned with food nutrition or food technology. Its coverage of the world-wide literature is quite complete, and thus makes it useful to all individuals concerned with food research.

C. O. CHICHESTER

FLAVOR RESEARCH AND FOOD ACCEPTANCE. *A Survey of the Scope of Flavor and Associated Research, compiled from Papers presented in a Series of Symposia given in 1956–57.*

Sponsored by Arthur D. Little, Inc. Reinhold Publishing Corporation, New York. $10.00. vi + 391 pp.; ill. 1958.

The sponsor of this series of symposia, Arthur D. Little, Inc., is one of the nation's important research laboratories devoted in great part to research on flavor.

The current trend toward multiple authorship of technical books seems to have reached some sort of apogee in this little volume, with no less than 41 authors participating. Truly the task of an editor facing so many styles and an almost equal number of subjects is frightening. In this instance, although limited by this new art form, the editor has done a creditable job in organizing and integrating the diversity of style and subject matter. The editor must indeed be a kindly person, for he has spared the blue pencil in many cases and allowed a good deal of individuality of style to each author. This provides some high points and, unfortunately, some low ones too.

The book is divided into 5 major sections, each of which borrows from some scientific discipline or technology and applies it to the problems of flavor research. The first section deals with the physiological and psychological aspects of flavor. The second section is concerned with laboratory flavor testing, wherein the major methods of sensory flavor evaluation used by the laboratory or small in-plant taste panels are examined. An exposition of consumer product testing is dealt with in Section Three. This covers the determination of product acceptance by consumer panels, as well as the importance of flavor in new product development. The fourth section concerns itself with specific applications of

product testing in industry. The fifth and final section treats the area of physicochemical research, and reviews the recent refinements in techniques and instruments which provide the flavor chemist with new micro-approaches to the chemical constitution of flavor.

One of the highlights of the book is a scholarly report of the work done by Alfred W. Weitkamp on Analytical Separation in the Study of Limonene Sulfides. In this work the author draws attention to the difficult task chemists face in attempting to separate complex mixtures such as those that comprise flavor. The humor of Robert K. Hower, Director of Research for the National Biscuit Company, is keenly emphasized in his article, Flavor Testing in a Baking Company. Persons working under autocratic executives will thoroughly enjoy this chapter.

The diversity of approaches to the chemical aspects of flavor is pointed up in two articles on strawberry flavor, one by Max Winter and the other by Joseph Corse and Keene P. Dimick. Both groups have given us much valuable information about the chemical constitution of strawberry flavor. William Stanley's careful and detailed examination of the coumarins in citrus is presented along with other less interesting studies in a review-like chapter on citrus flavors. Bill Stanley's work is of sufficient caliber that it should have been presented sans the review part. The field of flavor needs more research in this vein. Perhaps the chapter that presents the frustrations and tribulations of the flavor chemist most vividly is the one on Flavor Research on Cheese, by Harold W. Jackson. Nothing went right for this researcher until the day he discovered that chance plays a leading role in research. This chapter has, at least for one reader, some of the flavor (and I use the word advisedly) of O. Henry at his very best. The entire contents of the book are most ably summed up by A. J. Haagen-Smit.

As Loren B. Sjostrom states in the Preface of the book, "The series (symposia) is aimed to point up the diversity and interrelationship of the areas of flavor research, its progress and potentialities." If this be the goal of this volume, Sjostrom has succeeded. The book can be warmly recommended to those persons working tangentially to the field of flavor, but those who are actively engaged in flavor research will find it both too brief and elementary.

RICHARD A. BERNHARD

MANUAL OF NUTRITION. *Fourth Edition.* *Philosophical Library, New York.* $3.50. ii + 70 pp. 1957.

BIOCHEMISTRY

ANNUAL REVIEW OF BIOCHEMISTRY, *Vol. 26.* *Edited by J. Murray Luck, Frank W. Allen, and Gordon MacKinney. Annual Reviews, Palo Alto.* $7.00. ix + 768 pp. + 1 pl.; text ill. 1957.

Contents: Forty-five years of biochemistry (Peters); Biological oxidations (Mahler); Nonoxidative, nonproteolytic enzymes (Schwimmer); Proteolytic enzymes (Jandorf and Michel); Metabolism of lipides (Kennedy); Carbohydrate metabolism (de Duve and Hers); Water-soluble vitamins (Totter, Pt. 1, Greenberg, Pt. 2, and Novelli, Pt. 3); Fat-soluble vitamins (Blaxter); Nutrition (Portman and Hegsted); X-ray studies of compounds of biological interest (Kendrew and Perutz); Chemistry of proteins (Steinberg and Mihalyi); Amino acid and protein metabolism (Kamin and Handler); Nucleic acids (Chon and Volkin); Biochemistry of the steroid hormones (Dorfman); Haem pigments and porphyrins (Rimington); Clinical applications of biochemistry (Reinhold); Biochemistry in the U. S. S. R. (Stekol); Chemistry of the carbohydrates (Sowden); and Biochemistry of Muscle (Weber).

PROGRESS IN STEREOCHEMISTRY. *Volume 2.* *Edited by W. Klyne and P. B. D. de la Mare. Academic Press, New York; Butterworths Scientific Publications, London.* $8.80. vii + 323 pp.; ill. 1958.

This is the second in a series devoted to the review of physical methods and mechanisms of inorganic, organic, and enzymatically catalyzed reactions. An examination of the Table of Contents reveals subjects of interest to all types of chemists, and several of particular interest to biochemists. J. R. Marrack and Eva S. Orlans review steric factors in immunochemistry. Included are discussions of the structure of antigens and the structure of antigen-antibody aggregates. F. G. Mann reviews the stereochemistry of the Group V elements, which include two found in many biological chemicals, nitrogen and phosphorus. Although the compounds considered in the review are not frequently found in biochemical investigations, a knowledge of the stereochemistry of these compounds will be of great value to those determining the structures of nitrogen and phosphorus compounds found in biological systems. The review of the stereochemistry of homolytic processes (Gareth H. Williams) contains material of interest to those studying free radicals. J. C. Speakman discusses crystallography and stereochemistry and includes a brief discussion of the methods used as well as the results obtained in studies of compounds which are related to compounds of biochemical in-

terest. Three other reviews are concerned with organic chemist's problems: Stereochemistry of displacements at unsaturated centers (P. B. D. de la Mare); Steric effects on mesomerism (B. M. Webster); and Optically labile compounds (Margaret M. Harris). The stereochemistry of inorganic molecules is reviewed by J. F. Gillespie and R. S. Nyholm.

This series is edited by a biochemist and an organic chemist, and it is anticipated that future volumes will include more reviews of interest to biochemists as the techniques of stereochemistry become applied to biochemical problems. The present reviews include references to the current literature (1956–1957), of great value in fields which are advancing so rapidly. It is unfortunate that the editors did not include cumulative indices of both volumes of the series. That useful addition has become standard in most "series" types of publication.

LEOPOLD MAY

BIOCHEMICAL INVESTIGATIONS *in Diagnosis and Treatment. Second Edition.*

By John D. N. Nabarro. Little, Brown & Company, Boston. $6.00. xii + 299 pp.; ill. 1958.

The British author of this book has intended it "as a practical guide for internes and residents." It is an attempt to show how routine biochemical determinations can help in the solution of diagnostic problems and how they may be used as a guide in planning treatment. Numerous references and tables of "normal" values are included, but detailed descriptions of analytical procedures have been omitted. No major changes were made in this second edition. The index is divided into two parts: an index of investigations, and an index of conditions, diseases, and treatment.

This compact text is a valuable addition to the more comprehensive reference volumes on clinical biochemistry. In addition to the purpose stated by the author, I would zealously recommend it for collateral study in courses of medical biochemistry, clinical pathology, or internal medicine, as well as for use in schools of medical technology and nursing. Certainly most practicing physicians would find it helpful for reviewing current concepts of the biochemistry of clinical medicine.

The scope of the book includes both theoretical and practical considerations of fluid, electrolyte, acid-base, and calcium and phosphorus metabolism. Disturbances in the metabolism of protein and nitrogen, carbohydrate, and lipide are reviewed in relation with the laboratory evaluation of diseases of the gastrointestinal tract and pancreas, and of the liver and biliary tract. Chapter X, on biochemical examination of the urine, including routine tests of renal function, is especially recommended because of the basic importance of urinalysis in the practice of medicine. Brief but informative chapters on the cerebrospinal fluid, endocrine glands, vitamins, and poisoning lend additional merit to this useful synopsis of clinical biochemistry.

EUGENE W. RICE

STANDARD METHODS OF CLINICAL CHEMISTRY. *Volume II.*

By the American Association of Clinical Chemists; David Seligman, editor. Academic Press, New York. $5.50. xii + 217 pp.; ill. 1958.

The second volume in this series issued by the American Association of Clinical Chemists is a welcome sequel to its predecessor, published in 1953. The policy established with Volume I of having each method tested in the laboratory of a contributor and then critically evaluated in another laboratory of a checker has been continued. Procedures described are for calcium, cephalin-cholesterol flocculation test, chloride, cholesterol, total fatty acids in feces, gamma globulin, hemoglobin, 17-hydroxycorticosteroids, iron in serum, 17-ketosteroids, lipase, nitrogen by the Kjeldahl method, non-protein nitrogen, blood pH, alkaline and acid phosphatases, phosphatides in plasma, porphyrins, protein-bound iodine, sodium and potassium by flame photometry, bromosulfophthalein in serum, and urobilinogen. Alternative procedures to those found in Volume I for calcium, chloride, cholesterol, lipase, phosphatases, sodium, and potassium are included in this volume. The other methods are new to this series. The methods are presented in a reasonably uniform arrangement consisting generally of Introduction, Principle, Reagents, Procedure, Calculations, Discussion, and References.

The Editorial Committee has succeeded in significantly improving the current volume by standardizing the arrangement, describing more fully the preparation and stability of reagents, using significant figures, and freely interspersing notes throughout the text. In addition, pertinent literature references as well as ranges of values in healthy subjects and often in diseased persons, as established by these methods, have been included. In spite of the fact that it was necessary to use part of this book to correct some of the shortcomings of Volume I, it appears that Volume 2 paves the way for future editions.

This volume is recommended primarily to clinical chemists; but others such as pathologists, medical technologists, clinical investigators, chemists in other fields, and students will find in it valuable methods, ideas, facts, and references. It is to be hoped that subsequent members of this needed series will appear at shorter intervals than that between the first two volumes.

EUGENE W. RICE

ULTRAMICRO METHODS FOR CLINICAL LABORATORIES. *By Edwin M. Knights, Jr., Roderick P. MacDonald, and Jaan Ploompuu. Grune & Stratton, New York and London.* $4.75. viii + 128 pp. + 1 pl.; text ill. 1957.

The authors begin this small book with some brief comments on establishing a laboratory for quantitative microanalysis, including the selection of special equipment and the collection of blood samples. The remainder of the volume consists of microprocedures for sodium and potassium, calcium, chloride, phosphorus, carbon dioxide combining power, urea, glucose, total cholesterol, phosphatases, bilirubin, icterus index, thymol turbidity, cephalin-cholesterol flocculation, proteins (total, albumin, and globulins), paper electrophoresis, C-reactive protein, the Davies-Hinton and Mazzini flocculation tests for syphilis, and hematocrit. Descriptions of the analytical procedures are assembled uniformly under the headings Principle, Apparatus, Reagents, Procedure, Calculation, Calibration, Normal Values, Discussion, and References.

Most of the photometric methods are adapted from well-known "standard" macro-procedures by simply using from 0.01 to 0.2 ml of serum and proportionately small volumes of reagents. The addition of such basic microtechniques to the repertoire of the clinical laboratory is not difficult and requires little more than the use of certain common microchemical apparatus and glassware.

The main criticism of this book is that it is too expensive, considering its size and content. One could virtually duplicate the entire publication by collecting a few recent reprints of such investigators as W. T. Caraway, S. A. Kaplan, S. Natelson, A. E. Sobel, and M. Strumia, together with the descriptive brochures that accompany the purchase of the various items of equipment.

The excessive cost of the little manual possibly is due in part to the 19 figures it contains, many of which are of doubtful value. For instance, these pictures include 9 photographs of apparatus (2 each of the Kopp-Natelson microgasometer and the Gilmont microburette), one of a technician filling Bessey-Lowry micro cells, and a frontispiece showing simply a technician seated at a laboratory table!

EUGENE W. RICE

GAS CHROMATOGRAPHY. *A Symposium held under the Auspices of the Analysis Instrumentation Division of the Instrument Society of America, August 1957.*

Edited by Vincent J. Coates, Henry J. Noebels, and Irving S. Fagerson. $10.00. xii + 323 pp.; ill. 1958.

This symposium consists of 27 papers, which include discussions of the theory, instrumentation, and applications of this new analytical technique. The results are confined for the most part to those found with hydrocarbon mixtures. The investigation of biological systems will find little of direct application to his problems, but the papers on theory and instrumentation will be of great value. In addition to the references found at the conclusion of each paper, a bibliography of 489 references is included covering the years 1952–1957. This bibliography includes the titles of the articles and provides the reader with references to the particular analyses. This book is recommended to those who are using this method of analysis and to those who are investigating the usefulness of this technique in their own work.

LEOPOLD MAY

INFRARED ABSORPTION SPECTRA OF STEROIDS. *An Atlas. Volume 2.*

By Glyn Roberts, Beatrice S. Gallagher, and R. Norman Jones. Interscience Publishers, New York and London. $20.00. vii + 95 pp. + charts 309–760. 1958.

This is the second collection of infrared spectra of steroids. The same excellent style is continued in the presentation of the spectral curves. The present collection contains not only the spectra of steroids not included in the first volume, but also extensions of the spectral range of some steroids whose spectra were recorded in the first volume. The introduction has been enlarged and presents the reader with an extended discussion of intensity measurements and their uses. Very valuable additions to the usefulness of these two volumes are the table and chart of characteristic group frequencies. The authors have indexed the steroids found in both volumes alphabetically and according to functional groups. It is unfortunate that a conversion chart of wave length (μ) to frequency (cm^{-1}) was not included, since many instruments are still calibrated in μ and not in cm^{-1}, which is used throughout both volumes. The second volume is a continuation of the first, and both are necessary for investigators specifically studying steroids and other biological systems.

LEOPOLD MAY

CLINICAL ENZYMOLOGY.

Edited by Gustav J. Martin. Little, Brown & Company, Boston and Toronto. $6.00. viii + 241 pp. + 2 pl.; text ill. 1958.

The contents of this book are grouped into 7 chapters: Protein Biology, Chemistry of Enzymes Used Clinically, Biochemistry of Enzymes Used Clinically, Parenteral Use of Enzymes in Medicine, Diagnostic Use of Enzymes, Polymerases in Biology, and Recapitulation and Perspectives for Clinical Enzy-

mology. The book describes a promising new therapeutic approach to the treatment of disease—the parenteral administration of enzymes, their systemic actions, and their therapeutic effects.

The authors first provide a review of basic protein and enzyme chemistry. Especially interesting are the provocative views of Martin on biological relativity as it relates to chemotherapy and pharmacology. Next, a section is devoted to a description of the biochemical and pharmacological characteristics of enzymes which have been used clinically. The actual enzymes considered are trypsin, chymotrypsin, streptokinase, ribonuclease and deoxyribonuclease, hyaluronidase, and cholinesterase.

All of these discussions are directed toward a presentation of the clinical use of enzymes, which is illustrated by case reports and by summaries of the clinical literature. The diagnostic use of enzymes is given due consideration under this phase of enzymology, together with a brief review of the biologically important macromolecules—proteins, carbohydrates, and nucleic acids.

This book should be of special interest to the physician, biologist, student, or reader who wishes to orient himself quickly to the topic of the medical use of enzymes. Enzymologists, biochemists, and others well-trained in enzymology will not discover within this volume many enlightening facts or stimulating ideas. Perhaps some of these workers would be interested in *Clinical Enzymology* as a reference source.

Enzymes of known or suspected clinical utility which have so far received the most attention are in the main depolymerases, and are believed to affect tissue permeability. The results obtained with these enzymes have not been particularly promising. However, perspectives in the sphere of clinical enzymology may be bright, indeed. The field of clinical enzymology relates to the greater field of biocatalytic systems displaying the phenomena of "health and sickness,—life and death." In the practical sense, the polymerase-depolymerase system is the probable answer to aging, to collagen diseases, and to arteriosclerosis. Restoration of a normal enzymatic milieu ultimately may be achieved by the proper administration of enzymes. Enzymes will have then truly attained their role as the key to molecular diseases. Certain scientists (including Linus Pauling) even now foresee the day when many metabolic diseases will be treated by the use of *synthetic* "artificial" enzymes!

EUGENE W. RICE

ADVANCES IN CARBOHYDRATE CHEMISTRY. *Volume 13. Edited by Melville L. Wolfrom. Academic Press, New York.* $11.00. xii + 387 pp.; ill. 1958.

Since its inception in 1945, the *Advances in Carbohydrate Chemistry* has served as an excellent information medium for chemists and biochemists in regard to the progress and current trends in the diverse and intricate field of carbohydrate chemistry. As in the preceding series, Volume 13 contains discussions of topics of fundamental and timely interest. It opens with a chapter on the Formation and Cleavage of the Oxygen Ring in Sugars, by F. Shafizadeh, which deals with sugar-ring conformational analysis. The author considers the interconversion of the cyclic forms of a carbohydrate to its acyclic forms and to each other. The reactions are limited chiefly to the formation and hydrolysis of aldonolactones and aldosides and the deamination of amino sugars.

In the second article, the Lobry de Bruyn–Alberta Van Ekenstein Transformation, J. C. Speck is concerned with the progress of this reaction, which has been known for about 60 years. During the course of this time one or more of these reactions has been observed for nearly all of the known reducing sugars. The advances made in the elucidation of the mechanisms of these reactions and their metabolic roles have been well summarized. The author notes that during the past 8 years, 11 new enzymatic Lobry de Bruyn–Alberta Van Ekenstein reactions have been reported.

The Formazan Reaction in Carbohydrate Research, by L. Mester, is a review of the extensive studies of formazan chemistry, particularly of the various applications of the reaction to sugar hydrazones. The practical applications of the formazan reaction to the determination of reducing sugars and to the study of polysaccharide structure are discussed.

J. D. Crum, in a chapter on Four-Carbon Saccharide Acids, deals with products obtained from sugars by treatment with alkali in the presence of oxygen. These studies were initiated by J. U. Nef in the last century and have been continued by several of his students. The author is particularly concerned with J. W. E. Glattfeld's assiduous studies of the four-carbon acids.

Methyl Esters of 2-Amino-2-Deoxy Sugars, by R. W. Jeanloz, is another chapter in the series on the methyl ethers of the monosaccharides published in previous volumes. Interest in the preparation of the methylated amino sugars was stimulated in connection with the structural studies of oligosaccharides and polysaccharides, containing amino deoxy sugars.

The current interest in topics related to nucleic acid chemistry is reflected in a discussion by I. Goodman of the little-explored class of compounds of Glycosyl Ureids. It was suggested early in this century that synthetic compounds such as 1-ureido-D-glucuronic acid may occur under normal physiological conditions and are perhaps involved in animal metabolism. More recently the pyrimidine nucleotides, which have been synthesized from glycosyl ureids,

provide a basis for study and speculation as possible intermediates in the biosynthesis of nucleic acids.

F. Zilliken and M. W. Whitehouse summarize the information hitherto accumulated pertaining to the important group of compounds Nonulosaminic Acids. The existence of a family of amino sugars containing nine or more carbon atoms has only been realized within the last decade. The members of this group, neurominic acid and its acetylated derivatives, sialic acids, are widely distributed in natural mucopolysaccharides, mucoproteins, and lipopolysaccharides.

Under the topic Polysaccharide Hydrocolloids of Commerce, L. Stoloff attempts to "correlate the history, structure, function, botany and economics of these compounds so far as present knowledge permits, and to place in a new perspective those arbitrary divisions that have tended to separate starches, cellulose derivatives, sea plant colloids, gums, and mucilages into different categories." The author has undertaken a formidable task, and it may be said that he has succeeded within limits. However, it is doubtful whether the introduction of terms such as "polysacolloid" or "gelan" would help to clarify some of the confused issues.

In the article Alkaline Degradation of Polysaccharides, R. C. Whistler and J. N. Bemiller are chiefly concerned with the "β-alkoxy carbonyl mechanism" of degradation. This chapter includes a detailed discussion of the effects of alkali on reducing end-units, hydroxyl groups, and on oxidized polysaccharides. The final article, on Starch Nitrate, by C. V. Caesar, is an interesting account of the development of starch nitrate as an explosive.

The volume also contains an obituary of Carl Neuberg written by F. F. Nord. Carl Neuberg, who coined the term "biochemistry," is considered to be the "father" of that branch of science.

W. Z. Hassid

An Introduction to the Chemistry of Fats and Fatty Acids.

By F. D. Gunstone; foreword by T. P. Hilditch. John Wiley & Sons, New York. $6.00. x + 161 pp. 1958.

In 1924 the late E. F. Armstrong termed the fats "a neglected chapter in organic chemistry." The present flow of original articles on the chemistry and biochemistry of fats shows that this is no longer true as far as research is concerned. However, in respect to the teaching of the chemistry of fats and fatty acids in courses of organic chemistry, and to a lesser extent in biochemistry, the above description still holds to a surprising degree. From the standpoints of biology and biochemistry, a knowledge merely of the chemistry of formic and acetic acids, and of equations for the hydrolysis of tristearin and the reduction of oleic acids are no longer adequate.

This textbook on fat chemistry has been prepared for the use of honors students in organic chemistry and biochemistry. In the United States it can be highly recommended for secondary study in such courses, and as a primary text for graduate courses in the chemistry of the fats. The contents cover the structure and chemical properties of the fatty acids, and the physical and chemical properties of fats, with two final chapters on biochemical and technical aspects. The coverage of the subject is relatively complete and the treatment is logical and concise. The presentation of the chemical properties and reactions of fats is excellent. While designed as a textbook, the volume can serve as an introduction to this area for biologists and biochemists, or for review. A serious defect is that there are very few references to the original literature.

C. R. Treadwell

Progress in the Chemistry of Fats and Other Lipids. *Advances in Technology, Volume 5.*

Edited by R. T. Holman, W. O. Lundberg, and T. Malkin. Pergamon Press, New York, London, Paris, and Los Angeles. $14.00. viii + 338 pp. + 4 pl.; text ill. 1958.

This series has been very valuable to workers in the area of fats and to those desiring to keep abreast of theoretical and methodological advances in the field. Most of the reviews in previous volumes have dealt with the chemical and biochemical aspects of lipids. It was planned to publish reviews concerning technology in a separate series to be entitled, *Progress in the Technology of Fats*. However, it became evident that frequent volumes on technological advances were not justified. Also, the editors believe that a majority of those associated with the lipid field have interests that cut across both scientific and technological areas. For these reasons the present volume is composed of monographs which deal with recent advances in technology. It may be questioned whether those interested in the purely chemical and biochemical aspects of lipids will find the detailed descriptions of manufacturing processes, which are included in this volume, of interest.

The chapters cover such topics as standard methods in the fat and oil industry; technical aspects of the production of soap, marine oils, drying oils, and margarine. There are other chapters on the composition, properties, and utilization of fish oils. One chapter of general nutritional interest is on oilseed residues as a source of protein and amino acids in rations.

As with previous volumes in the series, the reviews are authoritative with adequate citations to the original literature.

C. R. Treadwell

DIE BIOCHEMIE DER TIERISCHEN GIFTE. *Einzeldarstellungen aus dem Gesamtgebiet der Biochemie. Band II.*

By Erich Kaiser and Heribert Michl. Franz Deuticke, Wien. Öst. S. 258.— viii + 258 pp.; ill. 1958.

The arrangement of this text is unusual. It consists of two parts, each of them dealing with different aspects of animal poisons. The first 169 pages contain a systematic survey of the species of the animal kingdom which produce poisons. In the remaining 56 pages of the text the enzymes discovered in animal poisons are discussed. Most of the first part is devoted to the few well-investigated poisons: bee venom, cantharidin, snake venoms, and toad poisons. It is disappointing to see that so little is known about the labile toxic substances of the bee and snake venoms or similar toxic materials in other animal species. The advent of modern analytical methods such as chromatography, paper electrophoresis, and countercurrent distribution should make research of this type much more promising at present than in the past. The book is well-written and contains more than 1000 references. It contains an index of the animal species mentioned in the book, a subject index, and an author index. It will therefore be a valuable source book for all who want to start research in the field of animal poisons.

F. HAUROWITZ

VENOMS.

By Eleanor E. Buckley and Nandor Porges. American Association for the Advancement of Science, Washington. $9.50 (AAAS members, $8.25). xii + 467 pp.; ill. 1956.

The *Quarterly Review of Biology* is just as tardy in noticing this volume as the publishers were in getting it to press since the symposium was held in December, 1954, and the publication date was December, 1956. Included are 61 papers by 85 contributors, who represented countries all over the world. The topics range from biochemistry to natural history. Among the venoms discussed are those from plankton, caterpillars, bees, scorpions, rays, fish, toads, reptiles, and mammals.

THE VISUAL PIGMENTS.

By H. J. A. Dartnall. John Wiley & Sons, New York. $6.00. vii + 216 pp.; ill. 1957.

"It is not the purpose of this book to deal with the visual aspects of the visual pigments, however, but to describe their physical and chemical properties and the methods that have been used to determine them." This quotation, from the author's introduction, quite accurately and concisely defines the goal and limitations of the book.

After a very brief discussion of the anatomy of the eye and the function of the visual pigments in vision, there follows a lengthy description of the the extraction methods and the various types of absorption and density spectra. Next come chapters on the various pigments and their photo products and the physical chemistry and structure of visual purple. Other chapters discuss the isomers of the visual pigments and the homogeneity of these products in solutions. The last chapter is an analysis of the recent methods of studying the properties of the unextracted visual pigments in cell suspensions and in vivo.

The many graphs and tables make the book valuable for reference. The beginner in the field will like the book because of the frequency of structural diagrams and the care with which the author has defined the terms used in the various equations. Each chapter is followed by its own bibliography. Although this method leads to frequent duplications, it does aid one in finding out what the pertinent literature is on a particular topic.

A better title for the book would be "The Vertebrate Visual Pigments," since none of the work on invertebrates is even alluded to. This is quite surprising. Squid visual pigment is known to have quite different properties from all vertebrate visual pigments, especially in the way that it is bleached and regenerated. Perhaps the second edition will correct this omission.

MYRON WOLBARSHT

DIE BLUTEIWEISSKÖRPER DES MENSCHEN. *Third Edition.*

By F. Wuhrmann and Ch. Wunderly. Benno Schwabe & Co., Basel and Stuttgart. $13.00. 499 pp. + 12 pl.; text ill. 1957.

This book is a comprehensive and thorough essay on the plasma proteins in health and disease. The authors have surveyed the world literature, but have drawn especially heavily from the English and German chemical and medical literature up to 1957 in preparing the third edition of this book, which first appeared in 1947. The organization and interpretation of the wide range of knowledge encompassed in this volume has benefited greatly from the authors' own extensive personal experience in both chemical and clinical aspects of the plasma proteins.

The authors first describe the chemistry of the normal plasma proteins, and then such abnormally occurring ones as the cryoglobulins, macroglobulins, myeloma proteins, and Bence-Jones proteins. They next discuss the chemical and physico-chemical methods of measuring and separating plasma protein

fractions, such as salting-out, ultracentrifugation, and electrophoresis, including the free method of Tiselius, paper electrophoresis, and the new method of immunoelectrophoresis in agar gel. The application of these methods to the diagnosis and understanding of many clinical diseases is discussed at length.

A final chapter deals with the clinical syndromes characterized primarily by marked abnormalities in the plasma proteins. These are classified as dysproteinemias (quantitative abnormalities of proteins normally present in the plasma), and paraproteinemias (the presence of proteins not normally found in serum), although it is recognized that this distinction may be artificial, since it is difficult by present methods of analysis to exclude the presence of normally occurring minute amounts of "paraproteins." Included in this chapter is a discussion of the relatively recent discovery of the congenital absence of ability to synthesize albumin, resulting in analbuminemia. Unfortunately, just as this book was in press, newer information on the mechanism of essential or idiopathic hypoproteinemia came to light, implicating the loss of plasma protein into the gastrointestinal tract with a consequent hypercatabolism in some cases, and possibly implicating an increased catabolic rate alone without gastrointestinal loss in other cases.

Fine illustrative electrophoretic patterns are provided throughout the text. However, despite the excellence of organizing and discussing a large body of information, this book suffers from an infelicitous style of writing, which doubly compounds the difficulty of an English-bred student in his problem of translation. However, that problem may be happily remedied in the very near future, when an English translation is forthcoming.

PAUL A. M. GROSS

THE CHEMISTRY OF TANNING PROCESSES.

By K. H. Gustavson. Academic Press, New York. $9.00. x + 403 pp.; ill. 1956.

The same author's book, *The Chemistry and Reactivity of Collagen*, and this one are meant to complement each other and to cover broadly the whole subject. Most of the volume deals with the chemistry of the various industrial tanning procedures and, therefore, is of limited interest to biologists. The final chapter, however, briefly treats biological and medical tanning reactions, such as: aromatic tanning invertebrates; possible tanning in the arteries and connective tissues of vertebrates with age; opsonins as tanning agents; formaldehyde reactions with toxins and viruses, and carcinogens and tanning of proteins. The author's approach to these biological subjects is provocatively different.

MICROBIOLOGY

BACTERIOPHAGES.

By Mark H. Adams, and five contributors. Interscience Publishers, New York and London. $15.00. xviii + 592 pp.; ill. 1959.

D'Herelle's book, which appeared in English translation in 1926, reviewed in detail the biological properties of bacteriophages obtained in the initial decade of research following his discovery. Work centered about the determination of the general nature of the lytic principle and its use in therapeutics continued at a prolific pace for a second decade before, in 1939, Ellis and Delbrück described the one-step growth curve technique, the cornerstone that has enabled bacteriophages to become the outstanding example of quantitative biology that they are today.

Although various aspects of bacteriophage research have been individually reviewed from time to time, the scope of each of these reviews is limited and, more often than not, is designed for an audience already versed in methodology and bacteriophage jargon. In contrast, Adams starts at the beginning. Through a strikingly simple sequence of clear and short steps he acquaints the reader with a modern view of bacteriophages. The uninitiated will have little trouble in grasping the clearly stated definitions, concepts, and theories, each placed in its proper historical and scientific perspective, that form the background to the intriguing problems now undergoing study in present-day research. Adams presents the reasoning behind each conclusion; and each fact is documented along with a guide to the literature for more extensive clarification where this might be desired by the reader. From the more than 6,000 papers in the literature on bacterial viruses, Adams has selected with a critical eye only those findings which are significant for understanding phages as organisms and infectious agents, as biological entities and tools for basic research upon fundamental problems. The first 3 chapters serve as a general survey of bacteriophages, the steps in the infective process, and quantitative methods used in bacteriophage studies. Throughout the book, quantitative methodology is continually emphasized, and the practical aspects of research technique are clearly stated. The most important methods are summarized in an appendix, a slightly appended reprint of an article by Adams, formerly published in 1950.

While suitable as an introduction to our knowledge of bacteriophages and the methods developed for their study, the book contains such a detailed and integrated picture that it will be of great value to anyone working on problems in, or allied to, virus

research. Adams has pointed out interrelationships and has striven for general conclusions wherever possible without forcing all observations into potentially erroneous generalizations. As one of the rare readers of the older literature, Adams is able to give credit where it is due; he calls attention to some long-lost endeavors providing data amenable to present-day interpretation. He presents a modern view of bacteriophages while staying on safe ground and avoids the fleeting vogues so characteristic of rapidly advancing research areas. Many comparative data are conveniently assembled into tabular form, and a fair index is included in the volume.

The more detailed discussions concentrate on the size and morphology of bacteriophage particles, effects of chemical and physical agents (including radiations) on them, and their chemical and serological constitutions. Host specificity and the process of adsorption are the concern of succeeding chapters, followed by attention to the cytological and biochemical aspects of bacteriophage multiplication. Additional discussions focus on various aspects of phage genetics: mutation, phenotypic variation, genetic recombination, and classification. The organization of these chapters, as well as cross references and comparisons, contribute to the clarity of the presentation.

At the time of Mark Adam's unfortunate death, in October, 1956, the book was in manuscript. The volume was completed only after a prodigious effort on the part of several competent workers, most notably A. D. Hershey. A further tribute to Adams is a chapter by J. S. Gots on chemical interference with virus growth, one of 4 chapters individually written in order to complete the content of the volume as Adams had originally outlined it. Gots, like many other microbial geneticists and students of bacteriophagy, received skilled instruction from Adams in one of the annual short summer courses at Cold Spring Harbor. Two chapters, by Jacob and Wollman, respectively on lysogeny and on bacteriocins, give brief and sound introductions to these areas. A final chapter, contributed by E. S. Anderson, surveys the uses of bacteriophages for bacterial typing.

PHILIP E. HARTMAN

HANDBUCH DER VIRUSFORSCHUNG. *Band 4 (III. Ergänzungsband).*

Edited by C. Hallauer and K. F. Meyer. Springer-Verlag, Wien. $35.25. xv + 688 pp.; ill. 1958.

In the early volumes of this work (1938–1944) emphasis was placed on methods and technics of studying viruses, and on general concepts and principles which the virus researcher might use. This was a commendable beginning in systematizing a mass of information that was largely heterogeneous until the early 1940's. Since then much progress has been made in integrating the science of virology. From the vantage point of 21 years later it is easy to appreciate the insight of the late Robert Doerr, who with C. Hallauer was a co-founder and the first editor of this work. The vision of the founders was expressed also in their choice of expert contributors from various parts of the world, giving the *Handbuch* an international character from its initiation. The third volume, which appeared in 1950, extended the original idea of providing systematized information applicable to investigative virology as a whole, but also contained reviews of specific problems. The present volume, in which this trend is even more apparent, is composed of two parts; the first is concerned with somewhat general topics, and the latter comprises reviews of research on five specific viruses or virus-groups. The editors indicate that future issues will contain similar monographs, in order to enable the *Handbuch* to take its place as a major reference work. (It should be realized that *Handbuch* does not translate directly to "handbook," at least for those to whom the latter word connotes a ready source of brief, concise information. "System" comes nearer to conveying the present meaning of the German term *Handbuch*.)

In the first portion of the book, in spite of the breadth of coverage, there was a wise choice of topics that in part complement one another, as is seen in the list of titles: Genetics of Animal Viruses (F. M. Burnet); Génétiques des Bactériophages (P. Fredericq); Viruses of Insects (G. H. Bergold); Arthropods as Vectors and Reservoirs of Phytopathogenic Viruses (K. M. Smith); Arthropods as Vectors and Reservoirs of Animal Pathogenic Viruses (W. C. Reeves); and Der Nachweis menschenpathogener Virusarten mittels der Gewebekultur (W. Klöne). The last named is particularly representative of the *Handbuch* as a source of information on methodology. Detailed descriptions are included of the principal methods used for virus culture in vitro, and of the results obtained with numerous viruses.

The special topics composing the second portion are the following: Les encéphalites saisonnières (P. Lépine and P. Goube de Laforest); Das Maul-und-Klauenseuche-Virus (H. Röhrer and G. Pyl); Columbia SK Group of Viruses (C. W. Jungeblut); The Virus of Poliomyelitis (S. Gard); and Die Coxsackievirus-Gruppe (H. Löffler).

These 11 chapters consist of scholarly and usually exhaustive treatments of their subjects by investigators active in the area of their respective topics. Each chapter has its own extensive list of references that cover publications through 1956. There is an index to the entire volume, and the table of contents includes all section headings and subheadings, so

as to increase the value of the book for reference. Illustrations are meager except in the chapters by Bergold, Klöne, and Jungeblut.

In a science that is developing as rapidly as virology, the need for a periodic review of many topics is very great. Although the various yearly review series fulfill this need in part, they cannot contain the wealth of detailed background information incorporated into a reference work such as this. On the other hand, such a compilation quickly becomes inadequate. (Genetic variation of animal viruses has been discussed in three different volumes of the *Handbuch*). Present plans for this work would seem to be a reasonable compromise, and promise to provide a valuable source of basic information on many aspects of virology.

The present volume represents an extremely useful and valuable book for virologists and students of viral diseases. For biologists in other fields, e.g., geneticists, entomologists, plant pathologists, and tissue culture workers, the first part of the volume especially will provide collected information on the contributions of virology to these subjects, and of these subjects to virology.

FRANCIS B. GORDON

PARASITOLOGY

BASIC CLINICAL PARASITOLOGY.
By David L. Belding. Appleton-Century-Crofts, New York. $9.00. x + 469 pp.; ill. 1958.

This is a concise, up-to-date summary of what the author conceives to be the more essential facts concerning parasitology and parasitic diseases in man. It is written more from a medical viewpoint than from that of the parasitologist and is intended for medical students and clinicians.

The compactness of this volume is remarkable. It is achieved by the liberal use of tabular arrays (42 of them) of comparative, summative, or otherwise related facts and of self-explanatory, well-wrought illustrations (118 figures), many of these being originals or adaptations, and by a masterly directness and economy of verbiage in the narrative component of the book.

The author treats his subject material by focusing his considerations generally on single species or on groups of closely related species in each genus of parasites. He names the disease produced and then proceeds with succinct accounts of the history and geodistribution of the organism, its morphology and physiology, life-cycle, pathogenicity (including symptomatology, pathology, and, where pertinent, immunology), its prognosis, treatment, diagnosis (these last two frequently by means of page references to relevant portions of later chapters where these subjects are dealt with collectively for all parasitic diseases), epidemiology, and control.

Spacewise, about 23 per cent of the pages are devoted to parasitic protozoa, 20 per cent to the roundworms, 7 per cent to the cestodes, and 13 per cent each to trematodes and arthropods. Thus about three quarters of the book is devoted to parasites and the diseases they cause. Another 15 per cent of the pages, comprising the last 3 chapters, is concerned with technical considerations of diagnosis and treatment. The first of these chapters deals mainly with the direct identification of parasites and contains helpful keys for this purpose. It also calls attention to certain serological, cutaneous, and chemical diagnostic procedures to supplement direct observations. The second describes the actual procedures of preparing, concentrating, and cultivating material to be examined, the techniques to be employed in serological and cutaneous tests, and the methods of examining intermediate and reservoir hosts. The third chapter consists of a digest of modern methods of treating parasitic infections and arthropod infestations, together with a descriptive list of drugs useful for these purposes. A brief discussion of insecticides and repellents used in preventing parasitic diseases is appended. References to literature are given at the end of each chapter, omitting the actual titles of the papers cited, in lieu of which brief indications of the subject matter are shown in parentheses.

This is not an encyclopedic or detailed work on parasitology and parasitic disease, nor is it just a guide or handbook in these fields. It is a skilfully presented concentrate of essential facts in these fields and is based, presumably, on the author's extended experience in teaching medical parasitology and related aspects of microbiology to numerous generations of students. It will be heartily appreciated not only by medical undergraduates and practitioners but by graduate students in parasitology, epidemiologists, preventive medicine officers, and laboratory workers who are concerned with the problems of parasitic disease. The author and publisher are to be congratulated on their achievement.

JUSTIN M. ANDREWS

GUIDE PRATIQUE DE MYCOLOGIE MÉDICALE.
By Jean Coudert. Masson & Cie., Paris. 6,000 fr. (cloth); 5,200 fr. (paper). xiv + 364 pp. + 8 pl. 1955.

A brief section on techniques of medical mycology begins this volume, followed by two large sections on diagnostic methods. The first of these consists of keys, a general key to the fungi, and a key to genera and species of pathogens in the various classes. The

last and largest section gives descriptions of each pathogenic species, from a quarter to a full page in length. This material is arranged under the following headings: clinical, gross, and microscopic characteristics; loci of infection; culture methods, animal tests, and epidemiology. Its logical arrangement, concise expression, and handsome appearance should make this a popular handbook.

HEALTH AND DISEASE

HEMOPHILIA AND HEMOPHILIOID DISEASES. *International Symposium.*

Edited by Kenneth M. Brinkhous. The University of North Carolina Press, Chapel Hill. $7.50. xxii + 265 pp.; ill. 1957.

This book contains the remarks of 62 participants and contributors who attended the International Symposium on Hemophilia and Hemophilioid Diseases in New York City, August 24–25, 1956. Kenneth M. Brinkhous has devoted his scientific career to the study of hemophilia and was thus quite prepared to organize an extraordinary symposium, which he has edited most expertly. All phases of hemophilia have been considered in it, including the various classifications, the antihemophilic factor, blood-clotting inhibitors, platelets, hemostasis and hemophilia, the inheritance of hemophilia and the hemophilioid states, the diagnosis of hemophilia, the management of hemorrhage in hemophilia and related diseases, hemophilic arthropathy, and the psychiatric and socio-economic aspects of hemophilia. Some sentences and even paragraphs I consider outright errors of fact; yet to be comfortable with such viewpoints is good mental dicipline, to be practiced as much as possible, for such is the nature of science reporting. In my opinion this book is another milestone in our progress in understanding a most difficult subject. It should be of value to the practicing physician, to those engaged in research on blood, and to anyone ready to broaden his knowledge of this subject. It presents an accurate picture of contemporary views on the subject.

WALTER H. SEEGERS

GLAUCOMA. *Transactions of the Second Conference, December 3, 4, and 6, 1956.*

Edited by Frank W. Newell. The Josiah Macy, Jr. Foundation, New York. $4.95. 245 pp.; ill. 1957.

This volume is the publication of papers contributed to a symposium held in December, 1956. The approach of the symposium was a fundamental one, ranging from a consideration of transport mechanisms to diagnostic methods. Included are the following papers: Mechanisms concerned with Aqueous Formation—Historical Background (Kronfeld); Introduction to Mathematical Formulation of Aqueous Dynamics (Kinsey); Mechanisms of Transport by Membranes (Berliner); The Glaucoma Problem (Goldmann); and Applanation Tonometry (Goldmann). The discussion which followed each paper is included, as well as an index and autobiographical sketches of the participants.

YELLOW FEVER VACCINATION. *WHO Monogr. Ser. No. 30.*

By K. C. Smithburn, C. Durieux, R. Koerber, H. A. Penna, G. W. A. Dick, G. Courtois, C. de Souza Manso, C. Stuart, and P. H. Bonnel. World Health Organization, Geneva. $5.00 (cloth). 238 pp.; ill. 1956.

Control of yellow fever by means of vaccination is summarized in this volume by means of the following contributions: Immunology of yellow fever (K. C. Smithburn); Preparation of yellow fever vaccine at the Institut Pasteur, Dakar (C. Durieux); Post-vaccination immunity with yellow fever vaccine of the Institut Pasteur, Dakar (C. Durieux & R. Koerber); Production of 17D yellow fever vaccine (H. A. Penna); Administration of 17D yellow fever vaccine, with special reference to Brazil (H. A. Penna); Vaccination by scarification with 17D chick-embryo vaccine (G. W. A. Dick); Time of appearance and duration of immunity conferred by 17D vaccine (G. Courtois); Mass yellow fever vaccination in French Africa south of the Sahara (C. Durieux); Mass vaccination against yellow fever in Brazil, 1937–1954 (C. de Souza Manso); Reactions following vaccination against yellow fever (G. Stuart); and International regulation of yellow fever vaccination (P. H. Bonnel). A select and classified bibliography of 378 references and an index conclude the book.

VIRAL AND RICKETTSIAL INFECTIONS OF MAN. *Third Edition.*

Edited by Thomas M. Rivers and Frank L. Horsfall, Jr. J. B. Lippincott Company, Philadelphia and Montreal. $8.50. xviii + 967 pp.; ill. 1959.

BACTERIAL AND MYCOTIC INFECTIONS OF MAN. *Third Edition.*

Edited by René J. Dubos. J. B. Lippincott Company, Philadelphia and Montreal. $8.50. xii + 820 pp.; ill. 1958.

The initial editions of these companion volumes gained wide respect for their lucid and accurate presentations of the various facets comprising medical microbiology. They have been valuable aids in medical teaching as well as convenient sources of reference for many other persons interested in an up-to-date survey of this broad area. So well con-

ceived were the first group efforts that they have required little reorganization in content or format at the present date. In contrast, rapid advances in medical microbiology, especially in the area of virus research, have necessitated complete rewriting and extension of many individual chapters. A new chapter, on chemotherapy, has been added to each volume. Furthermore, Dubos's volume reflects the increasing importance of immunology in the microbiological curriculum. The Rivers-Horsfall book has seen the greatest expansion, with new chapters on two new groups of viruses, the ECHO viruses and the adenoviruses. Both books treat biochemistry very briefly, but a review of the comparative biochemistry of virus infections now forms a valuable portion of the introductory chapters of Rivers-Horsfall. In general, the introductory chapters are better written and more cognizant of recent developments in microbiology than are the chapters which follow, on specific groups of organisms. Written by outstanding authorities who have made important contributions to the development of our understanding of etiological agents and infectious processes, the chapters of the two volumes, taken individually or viewed collectively, represent the finest introduction to medical microbiology existing today. Every alert and competent student who reads carefully even selected portions of these texts should gain an active interest in several microbiological problems. Adequate references are presented in a fashion generally amenable to further follow-up reading although, in some cases, one is unfortunately referred back to the 2nd editions for some of the titles. In contrast to their extreme usefulness for the exceptional student, one wonders if these voluminous texts will not become, for the majority of medical students, an occasional quick-reference supplement to hastily scribbled classroom notes. Nevertheless, the information is there, waiting for those teachers who can encourage their students to read and absorb, particularly with emphasis on the important general sections.

PHILIP E. HARTMAN

PHYSICO-CHEMICAL AND IMMUNOLOGICAL STUDIES ON THE VIRUS OF FOOT-AND-MOUTH DISEASE AND ITS HOST TISSUE MICROSOMES.

By Axel Randrup. Ejnar Munksgaard, Copenhagen. D. Kr. 1600. 68 pp. 1957.

ANESTHESIOLOGY AND RELATED PROBLEMS. *Ann. N. Y. Acad. Sci., Vol. 66, Art. 4.*

By C. R. Stephen and 24 other contributors. The New York Academy of Sciences, New York. $4.00 (paper). Pp. 841–1022; ill. 1957.

Anesthesiology and Related Problems consists of a series of papers given at the New York Academy of Sciences, which were concerned with 4 general headings: (1) Geriatric Anesthesia; (2) Controlled Respirations in Anesthesia; (3) Fluid and Electrolyte Balance in Surgery; and (4) Hypotension in the Operating Room.

Each of the four subdivisions contains papers by specialists in the field. All facets of surgical anesthesia have been authoritatively covered and discussed from a physiological, pharmacological, and surgical viewpoint. Of special interest is the contribution by Betty M. Cooper on the use of radioactive isotopes in the study of electrolyte balance in surgery. A most unusual paper, by J. B. Hickman and associates, relates to the use of mechanical respirators in patients with a high airway resistance. The entire volume represents a substantial contribution to the field of anesthesia, and is highly recommended to anesthesiologists and others interested in this field of medicine.

JOHN C. KRANTZ, JR.

CHRONIC ILLNESS IN A LARGE CITY: THE BALTIMORE STUDY. *Chronic Illness in the United States, Volume IV.*

Commission on Chronic Illness. Published for the Commonwealth Fund, Harvard University Press, Cambridge. $8.00. xxii + 620 pp.; ill. 1957.

This fourth volume is the counterpart of the third, which reported on a study of the prevalence of chronic illness and needs for care in a rural area, Hunterdon County, New Jersey. This fourth report deals with a similar study in Baltimore.

The study had five phases: (1) a door-to-door survey; (2) a clinical evaluation of a sample of the purported chronic illness discovered in Phase 1; (3) a multiphasic screening program; (4) estimates of "needs for care"; and (5) attempts at evaluating rehabilitation procedures on a selected group of handicapped persons. The first phase was conducted by expert interviewers of the Census Bureau in a 52-week period. The clinical evaluation in Phase 2 was performed by the Medicine I Clinic (now the Moore Clinic) of the Johns Hopkins Hospital. The screening program was conducted in the auditorium of the State Health Department, using procedures which did not require the subject to undress, and none of which required more than five minutes.

One major finding of this study is the surprisingly large number of chronic conditions diagnosed upon clinical evaluation. The weighted results indicated that 65 per cent of the non-institutionalized Baltimore population had one or more chronic conditions. An average of 1.6 conditions per person was diagnosed. With respect to some specific disease entities, the following unexpectedly high fre-

quencies were observed: heart disease, 9.6% of the population, plus an additional 6.6% of the population with hypertension without heart involvement; arthritis, in 7.5% of the population, osteoarthritis being more than twice as prevalent among women (9.3%) as among men (3.7%), and nearly twice as frequent among whites as among non-whites.

The other surprising result was the small proportion of all the conditions diagnosed by clinical examination which were detected by means of the household interview. Since some of these conditions could not have been detected by interview for a variety of reasons, the material was analyzed in terms of those conditions that ought to have been so detected; the percentage of such "detectable" conditions that were actually detected by the interview method was 30%. The finding has broad implications with respect to the use of the household interviewer method as a means of measuring morbidity in a community.

The screening program was largely unsuccessful, except from a methodological viewpoint, since only 29% of the designated sample responded. The estimates of the needs for care were found to be rather difficult to carry out because of difficulties in definition, etc. The rehabilitation project was not yet completed at the time of this report, but the authors were not hopeful with respect to the value of the data obtained.

The most outstanding feature of the report is the considerable discussion given to methodological questions. About 40 per cent of the volume consists of appendices concerned with the methodology of the household survey, clinical evaluation, multiphasic screening, etc. Much of the textual discussion concerns the various problems encountered in this rather intensive study, and the impressions of the study staff as to how future studies could be improved.

The Commission on Chronic Illness is to be congratulated on this report, which will no doubt remain essential reading for everyone interested in chronic diseases and for epidemiologists, statisticians, sociologists, and others who are concerned with field studies.

VICTOR A. MCKUSICK

THE TEACHING OF HYGIENE AND PUBLIC HEALTH IN EUROPE. *WHO Monogr. Ser. No. 34.*

By F. Grundy and J. M. MacKintosh. World Health Organization, Geneva. $5.00. 254 pp. 1957.

The authors, professors of preventive medicine and public health in Wales and England, report in this volume the results of their study of undergraduate and postgraduate education in public health and social medicine in 19 European countries. They discern three stages of development in public health practice and teaching. At the beginning of the bacteriological era, sanitation was developed as a technique of applying the new knowledge to the prevention of infectious diseases. Later, while maintaining these gains, public health moved out from under bacteriology and into the stage of community organization, characterized by dependence on special clinics, special hospitals, and public health nurses. Activities were focused on certain elements of the population, principally infants, children, and mothers, and on chronic infectious diseases such as tuberculosis and syphilis.

Although the second stage of development had developed strong social components, it dealt almost entirely with specific diseases and groups and did not attempt to cover the whole field of health and medical practice, as does the third stage, which is social medicine. This term defies precise definition; it is based on the study of social institutions—organized medical care plans, welfare services, social insurance, marriage, divorce, and war; personal factors that create or prevent peace and harmony, tension, frustration, love, hate, and anger; and the reasons why individuals and groups seek or refuse the benefits of the social institutions—and the use of that knowledge in protecting and promoting physical and mental health.

Mackintosh and Grundy distinguished between social medicine generally, which they feel should be taught as a separate phase of the undergraduate medical curriculum, and clinical social medicine, which they define as the application of social medicine principles to the diagnosis and treatment of individual patients. The latter not only should be taught in the department of social medicine, but its concepts should permeate all departments of the medical school, and it should be taught by the various departmental faculties, as well as the department of social medicine. The authors' model of a modern curriculum in social medicine adds medical sociology and statistics to the traditional subjects of environmental hygiene and sanitation, broadens the concept of epidemiology, and enlarges public health administration to cover the "newer" subjects of social and medical insurance, international health, and rehabilitation. The instruction in technical subjects that are far removed from the medical student's interest and the future doctor's responsibilities, and, it is assumed, the encyclopedic coverage that all too often make courses in public health a dreary business, are to be replaced by epidemiologic methodology and medical statistics.

Since teaching follows practice, in the professions at least, many countries have not yet reached a stage of social development that necessitates the teaching of social medicine, but in others, public health and social medicine have been made separate

departments in an effort to hasten the day when social medicine will be the only kind of public health subject taught to undergraduates, and the teaching will be along wholly academic lines.

Postgraduate instruction is viewed by Mackintosh and Grundy as primarily vocational, and in a general plan it is similar to the preparation for the practice of any other medical specialty. In Europe, much of the postgraduate training is given in medical schools or public health institutes, although public health schools as we know them in the United States are on the increase. Public health practice and teaching are almost exclusively the province of physicians in Europe. A few public health schools accept other members of the "team" —public health engineers, health educators, hospital administrators, and occasionally, public health nurses, but in most cases the nonmedical public health worker must obtain postgraduate training in the school of his or her basic training.

Descriptions of two to five pages each on undergraduate and postgraduate education in social medicine in the 19 European countries acquaint the reader with many novel and useful concepts, and methods of instruction.

As in other WHO monographs, the opinions expressed are those of the authors. In this case, however, the authors have drawn heavily on the papers read and the discussion at a pan-European conference in 1952 on undergraduate teaching, and on another, held in 1953, on postgraduate training, as well as their personal observations in most of the countries. For accuracy, they sent their descriptions of national programs to each of the 19 countries for comments and approval, and the entire volume was submitted to leading public health educators in eight countries representative of different patterns of medical education. This report is, then, authoritative in all but a narrow technical sense. It holds great interest and useful information for all who are concerned with teaching in public health schools, and especially for teachers of public health, the deans, and the faculties of the clinical departments of medical schools.

PAUL A. LEMBCKE

PSYCHOLOGY AND ANIMAL BEHAVIOR

BEHAVIOR AND EVOLUTION.

Edited by Anne Roe and George Gaylord Simpson. Yale University Press, New Haven. $10.00. viii + 557 pp.; ill. 1958.

Under the joint sponsorship of the American Psychological Society and the Society for the Study of Evolution, a conference was held in 1955 to see whether there was enough interest and pertinent information in the field of behavior and evolution to warrant further joint study. The results indicated that a second conference for the explicit purpose of producing a publishable symposium was desirable. At the conference each invited speaker presented a prepared paper. In the light of discussions at the conference each author revised his paper. This volume is a collection of the majority of these papers—yet it is more than just an assemblage. The means whereby the final drafts of the papers came into being were instrumental in giving the collection a measure of cohesion and unity. Unity is further imparted by the introductory chapter, the introductions to each part of the book, and the epilogue, all composed by the editors.

The book is divided into 5 parts. Part I, The Study of Evolution and Its Record, is composed of 3 chapters. In the first Simpson gives one of the clearest and most concise summaries of the present status of modern evolution theory. In the second Colbert discusses the possibility of deriving the behavior of extinct forms from a study of their morphology. In the third Romer attempts a summary of the phyletic evolution of vertebrate behavior. Part II, The Physical Basis of Behavior, consists of 5 chapters. Beach's discussion of the evolution of hormonal factors in male sexual behavior tends to support the idea that endocrine evolution is not an evolution of hormones but of the uses to which they are put. Caspari discusses the genetic basis of behavior; Sperry, the developmental basis of behavior. Pribram traces the differentiation of the forebrain in vertebrates and shows that comparative neurology can contribute to an understanding of the evolution of behavior. Bullock, in his treatment of the evolution of neurophysiological mechanisms, indicates that the present physiology of neurons, extrapolated, cannot account for behavior, but he denies dualism between brain and mind. Part III contains 7 chapters on categories of Behavior. In the first Nissen includes an approach to the problems of taxonomy of behavior and suggests a means of testing the hypothesis that there has been consistency in the direction of behavioral evolution. Bates discusses food-getting behavior, chiefly in insects and vertebrates, and concludes that the time is ripe for attempts at a synthesis in terms of behavioral systems like food-getting. Carpenter reviews concepts and problems of territoriality. The ethological approach to the study of behavior is presented by Hinde and Tinbergen in their chapter on The Comparative Study of Species-Specific Behavior. Harlow, in discussing the evolution of learning, confirms the general impression of over-all evolutionary increase in learning capacity while denying the existence of truly qualitative changes. Thompson examines the effect that evolution has had on social behavior and the effect that social

behavior has and may have on evolution. The evolution of behavior among social insects is treated by Emerson. Part IV, on The Place of Behavior in the Study of Evolution, consists of a chapter by Mayr on behavior and systematics, one by Spieth on behavior and isolating mechanisms, and one by Pittendrigh on adaptation, natural selection, and behavior. Part V, Evolution and Human Behavior, contains chapters on the biological elements of the evolution of human behavior by Washburn and Avis, on cultural processes and evolution by Huxley, on the relationship between the evolution of animals and the psychology of man by Freedman and Roe, and on cultural determinants of behavior by Mead. In the epilogue Simpson attempts with considerable success to tie the whole presentation together.

The area of knowledge covered by this volume is enormous. It could not hope to be exhaustive, yet it is a remarkably well-balanced and representative survey. The editors and contributors are to be commended in producing so well-organized and highly stimulating a study which, it is to be hoped, may represent a pioneer step toward future perceptive studies in this area.

V. G. DETHIER

AN INTRODUCTION TO THE BEHAVIOR OF INVERTEBRATES.

By J. D. Carthy. The Macmillan Company, New York. $8.00. xiv + 380 pp. + 4 pl.; text ill. 1959.

The subject of this book is mainly sensory physiology as studied by behavioral means. There is a chapter on responses to each category of stimulus, and a final brief chapter on whole patterns of behavior. Many topics integral to behavior are not discussed (e.g., learning, conditioning, drives, and the ethological viewpoint). Nor is sensory physiology discussed in any depth, for this could not conceivably be done without mention of the electrophysiology of the *Limulus* photoreceptors. Properties of the sensory receptors are presented only superficially. The bibliography lacks references to the articles in the books edited by Roeder and by Prosser, to a number of prominant review articles of the past five years, and to many noteworthy research papers on invertebrate behavior. The author has been uncritical of the experimental work he describes, and consequently the book cannot serve as a responsible introduction to the literature. The inclusion of the restrictive term "Introduction" in the title does not justify these deficiencies. Nor can these criticisms be mitigated by saying that the author had a point to make or a theory to develop, for there is no critical interpretation, no synthesis. The book can only be regarded as just another watered-down text. If the above criticisms are just, it is all the more regrettable, since there is a real need for a comprehensive review in English of invertebrate behavior. This lack will assure the book some popularity.

DAVID R. EVANS

THE EMPEROR PENGUIN *Aptenodytes forsteri* GRAY I. *Breeding Behavior and Development. Falkland Islands Dependencies Survey; Scientific Reports, No. 6.*

By Bernard Stonehouse. Her Majesty's Stationery Office, London. 10s. 6d. (paper). 33 pp. + 4 pl. + 1 folding chart; text ill. 1953.

THE ELEPHANT SEAL (*Mirounga leonina* LINN.). *II. General, Social and Reproductive Behaviour. Falkland Islands Dependencies Survey; Scientific Reports, No. 13.*

By R. M. Laws. Her Majesty's Stationery Office, London. 30s. (paper). ii + 88 pp. + 7 pl.; text ill. 1956.

THE BREEDING BEHAVIOUR AND REPRODUCTIVE CYCLE OF THE WEDDELL SEAL (*Leptonychotes weddelli* LESSON). *Faulkland Islands Dependencies Survey; Scientific Reports, No. 18.*

By A. W. Mansfield. Her Majesty's Stationery Office, London. 20s. (paper). 41 pp. + 6 pl.; text ill. 1958.

A COMPARISON OF BRAIN-INJURED AND NON-BRAIN-INJURED MENTALLY RETARDED CHILDREN ON SEVERAL PSYCHOLOGICAL VARIABLES. *Monogr. Soc. Res. Child Developm., Vol. XXII, Serial No. 65, No. 2.*

By James J. Gallagher. Child Development Publications, Purdue University, Lafayette. $2.50 (paper). 79 pp.; ill. 1957.

HUMAN BIOLOGY

THE BIRTH OF NORMAL BABIES.

By Lyon P. Strean. Twayne Publishers, New York. $3.95. 194 pp. 1958.

It is of interest to note that *The Birth of Normal Babies*, according to the dust jacket description, "concerns itself with those pregnancies that end in failure." It is quite unlikely that it will interest anyone except the layman, and it is extremely doubtful that any pregnant woman who intends to consult an obstetrician or reads any of the many reasonable books on childbirth would find it of any value. Actually the perusal of this book would re-

sult, assuming that the author is correct, in the very condition he believes to be the cause of most developmental abnormalities: emotional stress.

The book is a curious mixture of unsubstantiated theories and misconceptions, interspersed with a few reasonable ideas (some of which are based on Strean's recent experimental results and some of which have been accepted concepts for years, although presented as radically new). The basis of Strean's theories is that cortisone is a destructive agent produced in *abnormal* quantities by humans in stress situations (pregnancy is included as a stress situation) and the presence of excess cortisone during the development of an organ, tissue, etc., often results in its imperfect development. Except for this somewhat questionable theory Strean's scheme of things is confused and inaccurate. According to Strean, a genetic experiment conducted on any kind of nonhuman animal has little or no understandable relationship to human genetics. Not content with what he conceives to be a great moral truth, that man is not a "laboratory animal" (in fact not an animal at all) he states his own radiation theory: "While the dangers of X-rays and atomic fallout are real and may produce severe damage to those exposed to these powerful rays, there is no proof that mutation in the genes occur that would affect succeeding generations." It would behoove the author to read some of the literature on mutations since Muller's Nobel Prize-winning work on radiation in 1927. In fact, Strean's chapter on heredity is almost devoid of the most elementary understanding of genetics, heredity, or evolution. Perhaps the most reasonable statement in the whole chapter—and it is advice which merits the author's own attention—is that "A safe principle to follow is to leave genetics to the geneticist, and medicine to the physician." The author is neither.

Among other questionable items in the book are 60 case histories of abnormal births caused, according to the author, by stress situations. One example that he lists is malformation of the gut (pyloric stenosis) as a result of the mother having poison ivy. There is no end to Strean's confident assumptions. In addition to other areas of knowledge he writes as an authority in psychology, listing the following naive advice, found in a section entitled The Ten Commandments of Genesis, "Avoid severe emotional stress by learning to banish fear and by acquiring peace of mind. Trust your fellowman and your enemies will disappear."

The Birth of Normal Babies illustrates the result of extreme naiveté and as a consequence irresponsibility by a publisher and the author. Scientifically the book is at best amusing, but for a prospective parent it can only be detrimental. Certainly it is not instructive to anyone.

TIMOTHY MERZ

TRENDS IN GERONTOLOGY. *Second Edition.*
By Nathan W. Shock. Stanford University Press, Stanford. $4.50. viii + 214 pp.; ill. 1957.

The organization of this revised and expanded version of the 1951 edition is largely unchanged. About half of the discussion deals with trends in sociological, economic, and psychological aspects of human ageing. A chapter analyzes trends in the quantity and kinds of research on ageing and optimistically evaluates the progress that has been made. Another chapter, which few but the author could have written, describes current research in laboratories, all over the world, where research in gerontology is of primary interest. In ending, the author again examines the functions an Institute of Gerontology should perform. Like the well-known bibliographies of gerontology and geriatrics that Shock compiles, this book contains much information not available elsewhere.

DAVID R. EVANS

BIOMETRY

ELEMENTS OF MATHEMATICAL BIOLOGY.
By Alfred J. Lotka. Dover Publications, New York. $2.45 (paper). xxx + 465 pp.; ill. 1958.

The publishers deserve commendation for reprinting this influential book, one of continuing influence. It is a reprint of the 1924 edition of the *Elements of Physical Biology*, to which some corrections have been made and the author's bibliography appended.

DAVID R. EVANS

DE OMNIBUS REBUS ET QUIBUSDAM ALIIS

OUT OF THE TEST TUBE. *Fifth Edition.*
By Harry N. Holmes. Emerson Books, New York. $4.50. x + 313 pp.; ill. 1957.

Fortified by revisions and armed with new material—including chapters on atomic power and hydrogen bombs—*Out of the Test Tube* emerges in its fifth edition to defend and secure its position as a top-ranking popularization of chemical knowledge.

Holmes furnishes the reader with a historical panoramic sketch which unfolds to relate chemistry, in successive stages of development, to itself, to other fields of knowledge, and to every-day life. The general reader will find a great deal of information, stimulation for original thought, and considerable pleasure in this well-known book, which should also be a boon to beginning students of chemistry who sometimes forget or fail to relate their newly

learned facts and formulae to the general picture of chemistry.

JOE E. METTLER

TELEVISION IN SCIENCE AND INDUSTRY.
By V. K. Zworykin, E. G. Ramberg, and L. E. Flory. John Wiley & Sons, New York; Chapman & Hall, London. $10.00. xii + 300 pp.; ill. 1958.

Closed circuit television has become in recent years a useful enough tool in many areas of research and industry to justify a book on the subject. This book is divided into 5 parts: history, applications, the apparatus itself, some achievements of closed circuit systems, and a short forecast on the future of non-broadcast television. In the section on the apparatus the various types of camera tubes are discussed in considerable detail, both as to theory and practice. Also, most of the types of closed circuit television sets which are commercially available are described and critically analyzed—a very helpful section for anyone contemplating the use of such a set in his own work.

All of the authors are in some degree associated with the recent developments in television microscopy, and the book reflects their interest in this subject. Many of the pitfalls associated with the work in this field are mentioned, and also the great advantages that television can offer, particularly in the ultraviolet region. There is an appendix which compares the performance of vidicon and flying spot microscopes in the ultraviolet. This section should be studied by anyone interested in television microscopy. It marks the boundaries that can be hoped for in television microscopy with respect to resolution and noise level.

The book is generally well written, but some familiarity with the field of television is assumed because of the many undefined or poorly defined technical terms scattered throughout the text. However, this should not discourage anyone from reading the book; the other books on the same or related subjects are much more technical.

The volume contains many references to the original literature. The illustrations are copious and of very high quality.

MYRON L. WOLBARSHT

THE QUARTERLY REVIEW OF BIOLOGY publishes critical reviews of recent researches in all of the special fields of biological science. The contribution should present a synthesis or digest of the researches and a critical evaluation of them. A mere synopsis of the literature without evaluation or synthesis is not desirable.

Theoretical papers are published occasionally, especially when such papers (1) include a critical synthesis of the literature bearing on the theory and (2) are likely to promote further research in a given field.

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Material ordinarily taking the form of footnotes is set in small print and placed in the text and consequently should be written in a style so as to fit readily into the text. Acknowledgments are printed in the text in small type at the end of the article just preceding the List of Literature. Recent issues of the Quarterly should be examined for style as regards (1) section or subsection headings in the text, (2) literature citations in the text, and (3) List of Literature.

The subjects and authors of articles are selected by the Editors and members of the Advisory Board. Unsolicited articles which conform with the objectives of the Quarterly will be considered for publication.

A feature of the REVIEW is the section dealing with *New Biological Books*. In this department the book literature of different countries in the field of Biology is given comprehensive and critical attention.

The QUARTERLY REVIEW OF BIOLOGY is issued in March, June, September and December.

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